### Ligand-binding domain of the ultraspiracle (USP) protein

The invention relates to the spatial structure of the ligand-binding domain of the ultraspiracle protein, to the use of this structure for generating protein models of this protein in various conformations and of related proteins, and to methods of finding ligands of the ultraspriracle protein and of related proteins.

The ultraspiracle protein (termed USP hereinbelow) is the insect orthologue of the vertebrate retinoid X receptor (RXR). Like RXR, it belongs to the family of the nuclear receptors (NR). These nuclear receptors are located in the interior of the cell. They bind to responsive elements on the DNA as homo- or heterodimers and regulate the expression of genes. In order to be active they must bind specific small, frequently hydrophobic, ligands (for example steroids, retinoids, vitamin D). Nuclear receptors have a modular structure with functional domains for transactivation. DNA-binding and ligand-binding. While the DNA-binding domain of the nuclear receptors is highly conserved, the ligand-binding domains only show moderate homologies among each other. The spatial structures of various ligand-binding domains have already been determined (summary in 2) and allow an insight into the mechanism on which the activation is based, which comprises pronounced changes in the conformation of the ligand-binding domains. The binding of agonists leads to activation owing to the displacement of bound corepressors and the binding of coactivators, while the binding of antagonists prevents the interaction with the coactivator.

25

30

20

5

10

15

No spatial structures are available yet of insect nuclear receptors. In insects, for example the development from the larva to the adult insect is governed by nuclear receptors and involves the steroid hormone ecdysone and the isoprenoid juvenile hormone (3, 4, 5, 6). The ecdysone receptor, a nuclear receptor composed of two different subunits, EcR and USP, plays a key role in this process (7, 8, 9). It has been ET146894705US

July 20, 2001

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner of Patents and Trademarks, Washington, D.C. 20231

Donna J. Veatch

(Name of pe

10

15

20

25

known for a long time that the hormone ecdysone (in its active form 20-hydroxy-ecdysone) acts as ligand for the EcR subunit.

The ecdysone receptor constitutes an important insecticide target. If it is activated outside the windows in the period provided for insect development, this leads to severe damage or even to the death of the insects. The insecticidal action of ecdysone agonists is based on this mechanism (10, 11). Non-steroidal ligands of the EcR subunit which act specifically on Lepidoptera are already being used commercially as insecticides (12).

USP is an orphan receptor for which no ligand is known as yet. While various authors have assumed that USP constitutes a receptor for juvenile hormones, this has never been proven by actual experiments (9). Indeed, it has been assumed that USP has no ligand at all, as this is described for some other nuclear receptors known from animals

It was therefore an object of the present invention to provide the spatial structure of the ligand-binding domain (termed LBD hereinbelow) of the USP and to describe the possible ligand-binding pocket.

The object was achieved by providing a USP-LBD in crystalline form and by successfully carrying out the X-ray structure analysis of the crystals thus obtained.

The crystalline LBD according to the invention is preferably an LBD of the Heliothis virescens USP. The LBD according to the invention especially preferably has an amino acid sequence shown in SEQ ID NO: 1.

The subject-matter of the present invention is also a crystalline complex of a USP-LBD with a ligand. The LBD according to the invention preferably has the structure coordinates defined in Table 1. The three-dimensional structure was solved and fully refined with the aid of protein crystals which are accessible to X-ray structure analysis at high resolution by means of molecular replacement. Subject-matter of the present invention is thus also the three-dimensional structure of the USP-LBD which can be determined with the aid of these structure coordinates.

A ligand-binding pocket, into which – like in the case of the other known structures of nuclear receptors – the ligands bind, has been identified in the three-dimensional structure according to the invention of the USP-LBD described herein. This is the first actual confirmation for the fact that USP has a functional ligand-binding pocket.

Subject-matter of the present invention is furthermore a USP-LBD comprising a ligand-binding pocket which is defined by the amino acids LEU230, VAL238, PRO239, PHE242, LEU249, LEU291, ILE294, MET323, LEU331, GLN338, ALA339, VAL341, PHE345, SER431, HIS434, LEU435, PHE438 and LEU440 as shown in SEQ ID NO: 2 and Table 1.

Subject-matter of the present invention is furthermore a USP-LBD comprising a ligand-binding pocket defined by the amino acids LEU230, VAL238, PRO239, PHE242, PRO245, VAL246, LEU249, CYS250, GLY253, ASN287, LEU290, LEU291, ILE294, MET323, LEU325, LEU331, SER335, ALA336, GLN338, ALA339, VAL341, ILE344, PHE345, VAL348, SER431, HIS434, LEU435, PHE438 and LEU440 as shown in SEQ ID NO: 2 and Table 1.

25

30

5

10

15

20

Subject-matter of the present invention is furthermore a USP-LBD comprising a ligand-binding pocket which is defined by the above-described amino acids and in which one or more of these amino acids are mutated. These are preferably conservative mutations, where an amino acid is exchanged for an amino acid with similar physical properties.

5

10

Such conservative substitutions encompass variations in which an amino acid is replaced by another amino acid from amongst the following group:

- Small aliphatic residues, nonpolar residues or residues of little polarity: Ala, Ser, Thr, Pro and Gly;
- 2. Polar, negatively charged residues and their amides: Asp, Asn, Glu and Gln;
- 3. Polar, positively charged residues: His, Arg and Lys;
- 4. Large aliphatic nonpolar residues: Met, Leu, Ile, Val and Cys; and
- 5. Aromatic residues: Phe, Tyr and Trp.

Preferred conservative substitutions can be seen from the following list:

Original residue	Substitution
Ala	Gly, Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Ala, Pro
His	Asn, Gln
Ile	Leu, Val
Leu	Ile, Val
Lys	Arg, Gln, His
Met	Leu, Tyr, Ile
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Trp	Tyr, Phe
Tyr	Trp, Phe
Val	Ile, Leu

The three-dimensional structure described herein of a USP-LBD is of great importance for the search for ligands with practical application. Such ligands can be used, for example, as insecticides with a novel mechanism of action. The ecdysone/juvenile hormone-governed development is only found in invertebrates and not in vertebrates; thus, it constitutes an insecticidal mechanism which is safe for the user and the environment.

10 Using the three-dimensional structure according to the invention of the USP-LBD, databases which contain the structures of a large number of compounds can be screened with the aid of established, automated computer protocols (virtual screening). Algorithms such as FLEXX (13) or GOLD (14) are examples which can be used for virtual screening. With this procedure, compounds can be identified whose three-dimensional structure makes it possible to enter the binding pocket and to bind there, for example by forming hydrogen bonds, by hydrophobic interaction, by electrostatic interactions, by van-der-Waals interactions or by dipole interactions. The compounds identified thus can be synthesized and then used as, for example, insecticides or as effectors in expression systems (gene switch) based on the USP.

Another application of the three-dimensional structure according to the invention of the USP-LBD is the generation of new ligands. To this end, structural formulae for new ligands are generated on the computer using this structure and with the aid of established *de-novo* design programs, and these new ligands can enter the binding pocket, where they can bind, for example by forming hydrogen bonds, by hydrophobic interaction, by electrostatic interactions, by van-der-Waals interactions or by dipole interactions. Examples of *de-novo* design programs which are possible are LUDI (15), LEGEND (16) or GROW (17). Compounds generated thus can be synthesized and then also be used as, for example, insecticides or as effectors in expression systems (gene switch) based on the USP.

20

25

30

5

10

15

The three-dimensional structure according to the invention of the USP-LBD also makes it possible to predict the three-dimensional structure of a USP-LBD from other organisms by means of modelling methods. Such protein models can be used in the same manner as the three-dimensional structure solved herein. Comparison of the differences in the amino acid sequences makes it possible to predict differences in the ligand-binding pockets of various organisms. This is of use when specific ligands are searched for for specific organisms, or, conversely, when it is precisely unspecific ligands that are searched for. In addition, the three-dimensional structure according to the invention can be used for establishing protein models of other nuclear receptors with related sequences.

10

15

The present invention encompasses in particular the following subject matters and methods:

A computer-readable data storage medium comprising a data storage material on which the structure coordinates of an LBD according to the present invention are stored.

A computer-readable data storage medium in a form which makes it possible to generate a three-dimensional image of an LBD according to the present invention on a computer screen.

A method of generating protein models of USP-LBDs, characterized by the computer-aided generation of a three-dimensional image of an LBD according to the present invention.

A method of generating protein models of USP-LBDs in an agonistic conformation, characterized by the computer-aided generation of a three-dimensional image of an LBD according to the present invention in an agonistic conformation.

20 A method of generating protein models of nuclear receptors which have homologies with USP-LBDs, characterized by the computer-aided generation of a threedimensional image of an LBD according to the present invention with a mutated amino acid sequence.

25 A method for generating protein models of nuclear receptors which have homologies with USP-LBDs in an agonistic conformation, characterized by the computer-aided generation of a three-dimensional image of an LBD according to the present invention with a mutated amino acid sequence in an agonistic conformation.

30 A method of finding USP ligands, characterized by the following steps:

10

15

20

25

- the computer-aided generation of a three-dimensional image of an LBD according to the present invention, and
- (b) the computer-aided (virtual) screening of databases which contain structural data of chemical compounds for those structures which are capable of undergoing specific interactions with an LBD according to the present invention.

A method of finding USP ligands, characterized by the following steps:

A inction of finding our figures, characterized by the following steps

- the computer-aided generation of a three-dimensional image of an LBD according to the present invention, and
- (b) the computer-aided modelling of chemical compounds with structures which are capable of undergoing specific interactions with an LBD according to the present invention.

A method of finding USP-LBD ligands in an agonistic conformation, characterized by the following steps:

- the computer-aided generation of a three-dimensional image of an LBD according to the present invention in an agonistic conformation, and
- (b) the computer-aided (virtual) screening of databases which contain structural data of chemical compounds for those structures which are capable of undergoing specific interactions with an LBD in an agonistic conformation.

A method of finding USP-LBD ligands in an agonistic conformation, characterized by the following steps:

10

15

20

- the computer-aided generation of a three-dimensional image of an LBD according to the present invention in an agonistic conformation, and
- (b) the computer-aided modelling of chemical compounds with structures which are capable of undergoing specific interactions with an LBD in an agonistic conformation.

A method of finding active compounds for crop protection, in particular chemical compounds which, owing to binding to an LBD according to the present invention, bring about the activation or inhibition of USP, with the following steps:

- (a) carrying out one of the abovementioned methods for finding USP ligands,
- (b) synthesizing the compound(s) identified as ligands, and
- (c) detecting the bioactivity of the compound synthesized in step (b) by transactivation assays, displacement assays or bioassays.

A method of finding active compounds for crop protection, in particular chemical compounds which, owing to binding to an LBD according to the present invention in an agonistic conformation, bring about the activation or inhibition of USP, with the following steps:

- (a) carrying out one of the abovementioned methods for finding USP-LBD
   ligands in an agonistic conformation,
  - (b) synthesizing the compound(s) identified as ligands, and
- (c) detecting the bioactivity of the compound synthesized in step (b) by transacti vation assays, displacement assays or bioassays.

09909555.072001

5

10

15

A method of finding effectors for systems for the inducible expression of target genes by means of USP, with the following steps:

- (a) carrying out one of the abovementioned methods for finding USP ligands,
- (b) synthesizing the compound(s) identified as ligands,
  - (c) applying a compound synthesized in step (b) to host cells or host organisms which contain a USP-based expression system, and
  - (d) detecting an induction or inhibition of the expression system.

The use of an LBD according to the present invention or of a computer-readable data storage medium according to the present invention for finding active compounds for crop protection or effectors for the controlled expression of target genes in host cells or intact host organisms.

The present invention is described in greater detail with reference to the examples which follow.

15

20

25

## Examples

## Example 1

# 5 Protein expression and purification

The Heliothis virescens USP-LBD (AS Val-205 to Met 466) was cloned in a pET-15b expression vector as N-terminal fusion protein with a His-tag and overexpressed in the E. coli strain BL21(DE3). The cells were cultured in 2x LB medium at 37°C and induced for 2 hours with 0.8 mM isopropyl-β-D-thiogalactopyranoside at 24°C. The protein extract was purified over a cobalt chelate column with subsequent gel filtration over a Superdex 200 16/60 column. The His-tag was then removed by digestion with thrombin and the protein was removed by gel filtration. A homogeneous monomeric protein species was present in the solution and was confirmed by means of SDS and native polyacrylamide gel electrophoresis and by denaturing and native electrospray ionization mass spectrometry.

## Crystallization

Crystallization was effected by gas diffusion on hanging drops. The protein concentration employed was 3-9 mg/ml. Crystals 200 x 200 x 400 mm³ in size formed within 10 days from a solution containing 10% of polyethylene glycol (PEG) 4000, 50 mM Tris (pH 7.5), 100 mM NaCl and 5 mM dithiothreitol and which was equilibrated in the reservoir against a solution of 20% polyethylene glycol (PEG) 4000 and 100 mM Tris (pH 7.5). The crystals belong to the tetragonal P4322 spatial group with one monomer per asymmetric unit. The parameters of the standard cell are a=58.21 Å, b=58.21 Å, c=144.69 Å and  $\alpha=\beta=\gamma=90^\circ$ . The solvent content is 32%, and the B-factor estimated in the Wilson Plot is 27 Ų.

10

15

20

25

30

### Data gathering, structure determination and refining

Crystals were immersed briefly in a 10% glycerol solution and shock-frozen in liquid nitrogen. The native data set was produced with a single crystal at measuring station ID14-EH2 at the ESRF (Grenoble, France). The data were processed with the aid of HKL programs (18). The crystal structure was solved by the molecular replacement method (19) by means of a partial hRXRα structure (20) as search model. A poor solution was achieved with a correlation of 24.8% and Rfree=54.5% after refining as a rigid body. The phasing power of the model was low and required a number of manual generateing cycles with O (21). The wARP method (22) was used to verify the correctness of the partially-built structures. Refining was performed with CNS (23) using a maximum likelihood target function and solvent correction. Cycles of manual modelling and least-square minimization with subsequent simulated annealing and individual anisotropic B-factor refining gave rise to the final model. Solvent molecules were contoured in an  $F_{\text{o}}-F_{\text{c}}$  map at a surface of  $3\sigma.$  The final model, refined to a resolution of 1.65 Å, comprises 246 amino acid residues, 259 water molecules and one ligand molecule. A large portion of the connecting loop between Helix H5 and the beginning of the β-pleated sheet (amino acid residues 306-315) and the C-terminal extension of H12 (amino acid residues 459-466) could not be shown, owing to the poor electron density in these regions. The quality of the final model was checked with Procheck (24).

Characterization of the USP-LBD crystals by electrospray time-of-flight mass spectrometry (ESI TOF-MS) under natural conditions shows a heterogeneous mass distribution around 740 ± 50 Da in addition to the peak of the pure protein (30.2 kDa). This suggested that a ligand is present which is bound in LBD. The presence of a ligand was confirmed by the electron density. Various complementary techniques were used to characterize the ligand. The ligand, which is located in the binding pocket of the USP-LBD, was characterized as a phospholipid molecule. A phosphatidylglycerol or a phosphatidylethanolamine or a phosphatidylcholine would match the crystallographic data and are consistent with the results from mass

spectroscopy and chemical analysis. These amphiphilic molecules have a head group consisting of a phosphorylglycerol or a phosphorylethanolamine group and a tail of two different fatty acids which are bonded to the glycerol-3-phosphate by ester bonds. A detailed description of the ligand and its interactions with the USP-LBD residues are given in the following text.

#### Example 2

5

10

15

20

25

30

## Architecture of the Heliothis virescens USP-LBD

In general, the architecture of the USP-LBD exhibits canonic NR folding with 11 αhelices (H1, H3-H12) and two short β-strands (s1-s2). This structure was compared with two other crystal structures which have essential properties of NRs and which are closely related to the Heliothis virescens USP: the binding pocket of agonistbound RXR $\alpha$  (hRXR $\alpha$ /9-cis RA) and antagonist-bound mice RXR $\alpha$  (msRXR $\alpha$ /oleic acid). Superposing the USP-LBD with the structure of the holo-RXRα-LBD was carried out with the aid of a least-square fit [LSQ]. In total, the secondary structural elements of the USP-LBD are capable of reasonably good superposition by those of the holo-RXRα-LBD. The root mean square deviation (r.m.s.d.) is 1.22 Å for 183 out of 246 superposed Ca atoms. Seven helices are accessible to reasonably good superposition (r.m.s.d. 1.13, 0.88, 0.57, 1.18, 0.67, 0.69, 0.75 Å for H4, H5, H7-H11). The C-terminus of H1 is curved by approximately 2 Å relative to helix H3, and its r.m.s.d. is 1.63 Å. H3, H6 and the β-pleated sheet show larger deviations. The structure of the USP-LBD demonstrates that the activation helix H12 assumes a conformation which is similar to that of the antagonist-RXRa. The antagonistic AF-2 conformation of the USP-LBD is discussed further below.

The connecting loop L1-3 of most NRs usually behaves as a highly flexible region. In the case of hRXRa, the crystal structures of both the apo and the holo conformations show substantial differences in the regions which connect helices H1 and H3. In the holo-LDB structure, L1-3 consists of an extended loop which extends

10

15

20

25

30

beyone the  $\beta$ -pleated sheet and a  $\Omega$ -loop. The apo form contains an additional helix in this region which unfolds in the holo-form. During the transition from the apoform to the holo-form, L1-3 undergoes substantial movement. In particular, the  $\Omega$ -loop becomes oriented towards the opposite side of the protein centre. As has been proposed on the basis of the comparison of the two structures, L1-3 might act as a molecular spring which accompanies the conformational changes which are linked to ligand binding. For the ligand-bound RAR $\gamma$ -LBD, the conformation of L1-3 resembles that of the holo-RXR $\alpha$ . Interestingly, L1-3 for ER-LBDs follows a path other than in the case of holo-RXR $\alpha$ . It runs between helix H3 and the  $\beta$ -pleated sheet, packed tightly to the protein centre.

In the case of the USP-LBD, L1-3 assumes none of the conformations which are otherwise found in the other NRs. Its course (Val-220 to Pro-239) was derived unambiguously from the electron density maps. Only few residues at the beginning of the loop, namely Asp-222, Pro-223 and Ser-224, were treated as alanins owing to the poor electron density of the side chains. The temperature factors of these residues are therefore higher (60-64 Ų) than those of the other amino acids of L1-3 (on average 36 Ų over L1-3). The first residues of L1-3 form a path which crosses helix H3 in the region Gln-256 to Val-262. The next residues (Glu-226 to Pro-234) form an extended loop which runs along H3, and, finally, the last five residues of L1-3 (Asp-235 to Pro-239) form a loop which has substantial similarity with the  $\Omega$ -loop observed in the LBDs of RXR $\alpha$  and RAR $\gamma$ . L1-3 assumes quite a tight conformation which makes it possible to establish direct contacts with the residues of helices H3, H11 and H12 and to stabilize their actual positions. This is important in as far as these helices are those structural elements which are subject to the greatest conformational changes owing to ligand binding.

The particular conformation of L1-3 is not based on crystal packing effects. In the region of the loop L1-3 of RXR $\alpha$ -LBD, the USP-LBD interacts with its symmetry-equivalent molecule via the  $\beta$ -pleated sheets. It is extremely likely that this interaction takes place since L1-3 does not already occupy this region when the protein is

10

15

20

25

in solution. If, owing to packing effects, L1-3 would be forced to swing and to move away from a conformation which is similar to the actual conformation of  $RXR\alpha$ , several elements of the secondary structure would have to move drastically from this hypothetical conformation to their final position. It is therefore highly unlikely that this drastic reorganization of all of the LBD takes place, in particular because L1-3 lies in a region of the LBD in which L1-3 establishes very specific interactions with adjacent elements of the secondary structure.

Directly linked to loop L1-3, helix H3 differs from its counterparts in RXRa both regard to length and with regard to the position of the N- and C-terminal portion . In Heliothis virescens USP, H3 starts at Pro-240 and is therefore one turn longer than H3 in the ligand-bound RXRα (start at RXRα-Pro-264). The residues of H3 in the middle portion of the helix assume almost identical positions compared with the positions of the corresponding residues in the apo- and holo-RXRa-LBDs. However, both N- and C-terminal regions are curved towards the exterior of the protein centre. The N-terminal region of H3 (Pro-240 to Cys-250) is shifted substantially towards H11. It is tilted by approximately 24° in comparison with the same region in the holo-RXRα (approx. 7.2 Å between USP-Pro-245 and holo-RXRα-Pro-264). This position lies between those of the N-terminal regions in the apo-RXRα and the holo-RXRα-LBD structure. The outwardly curved C terminus of H3 (by approx. 10°) has effects on the arrangement of the adjacent loops L3-4 and L8-9. Loop L3-4, which is part of the signature region of NRs, is shifted laterally by approximately 1.8 Å and curved towards L8-9, while loop L8-9 itself is shifted outwardly by approximately 1.5 Å.

Example 3

## The ligand-binding pocket

30 The ligand-binding pocket of Heliothis virescens USP is formed by residues of loop L1-3, helices H3, H5, H6 and H7, the β-pleated sheet and loop L11-12. As described

10

15

20

above, the N-terminal portion of helix H3 is markedly shifted outwardly compared with its opposite number in RXR $\alpha$ . Two other secondary structures which contribute to the binding pocket also differ from those in RXR $\alpha$ : 1) Helix 6 has moved inwardly by approximately 1.9 Å, and 2) the curvature of the  $\beta$ -pleated sheet points towards H1. The shift of the three structural elements which this entails lead to a widening of the ligand-binding pocket compared with that of the RXR $\alpha$ -LBD. The edge of the binding pocket is formed by the  $\Omega$ -loop of L1-3, the N terminus of H3 and H6, while in the case of RXR $\alpha$  the opening of the pocket is formed by loop L11-12 and H6. At its opening, the binding pocket is approximately 13.5 Å wide (distance between Lys-241 in H3 and Gln-338 in H6). This opening is much wider than in the case of RXR $\alpha$  (7,1 Å from Pro-264 in H3 to Ala-340 in H6). The topology of the ligand-binding pocket is relatively unusual with a gap between H3 and H6. In RXR $\alpha$  and other NRs, this region forms fixed contacts with the connecting loop L1-3. The volume of the cavity of the USP-LBD achieves that of the hRXR $\alpha$ -LBD by a factor of 2.5 (1256 Å $^3$  in the case of USP compared with 489 Å $^3$  in the case of hRXR $\alpha$ ).

## Example 4

# The putative ligand of USP in the crystal structure

Unexpectedly, the ligand-binding pocket of Heliothis virescens USP contains a molecule which was copurified and cocrystallized together with the USP-LBD. The fit of the electron density agrees well with the characterization of the molecules by mass spectroscopy and analytical chemistry. Similarly, recent crystallographic studies of the heterodimeric RARα/RXRα-LBD show an E.coli-endogenous oleic acid (C18) or a similar compound (stearic (C18) or palmitic (C16) acid) in the RXRα subunit. Even though this molecule is not the natural ligand of vertebrate NR,

it induces and stabilizes an antagonistic AF-2 conformation which in all probability is very similar to the actual antagonist-bound  $RXR\alpha$ .

10

15

20

25

30

In the present case, the best fit of the electron density was assumed with the assumption of a phospholipid whose first tail consists of a fatty acid with a length of 18 carbon atoms at C1 and a second chain at C2 which is 16 carbon atoms in length. The longer fatty acid of the two has a relatively twisted shape with two largish peaks, while the other fatty acid assumes a more normal form within the pocket. The tail of the phospholipid is hidden within the ligand-binding pocket. The glycerol moiety and the two fatty acids form van-der-Waals contacts with the residues in L1-3 (Leu-230, Val-238), H3 (Phe-242, Leu-249), H5 (Leu-291), L6-7 (Ala-339), H7 (Phe-345), H11 (Ser-431, His-434, Phe-438) and L11-12 (Leu-440). The head group of the phospholipid is positioned at the front at the opening of the pocket between H3 and H6. A strong hydrogen bond with Gln-338 (H6) is formed by the carbonyl group of the phosphorylglycerol in the case of phosphatidylglycerol and by the amino group of the ethanolamine in the case of phosphatidylethanolamine. In addition, an oxygen of the phosphate group is bound to a residue L1-3 (Cγ of Pro-239) by a hydrogen bridge.

It is assumed that the phospholipid found herein constitutes no natural USP ligands. However, it is shown unambiguously that USP ligands exist.

The residues which interact with the ligands are highly conserved within lepidopteran USPs, with the exception of Ser-431, which is replaced by a cysteine in msUSP. In contrast, among the 16 residues of the RXRα-LBD which interact with 9-cis RA, only 3 of the corresponding USP residues interact with the phospholipid (Leu-249, Ser-431 and His-434). The reason for this behaviour is mainly the different position of the ligands in the corresponding pockets. The 9-cis RA is very deep within the pocket, where its carboxylate group forms a salt bridge to Arg-316 of helix H5 of the hRXRα. In contrast, the phospholipid does not penetrate far into the inside of the pocket. For example the tail of the longer fatty acid lies approximately at atom C9 of 9-cis RA in hRXRα-LBD, while the tail of the other fatty acid extends almost to the β-ionone ring of 9-cis RA. As a consequence, Arg-297 does not participate in the anchorage of the ligand, as is observed in the case of the agonistic RXRα-, RARγ-

and other NR-LBDs. Nevertheless, it assumes almost the same position as Arg-316 of the holo-RXR $\alpha$  and not the position of the apo-RXR $\alpha$  conformation, which is exposed to the solvent. Instead of interacting with the ligand, Arg-297 forms hydrogen bonds with the backbone carbonyl group of Leu-325 ( $\beta$ -pleated sheet) and participates in a hydrogen bond network with Leu-290 (H5) and the side chain of Gln-256 (H3), with participation of water. In particular, two water molecules which are positioned spatially approximately at the two oxygen atoms of the carboxylate group of 9-cis RA participate in these interactions.

### Example 5

5

10

15

20

25

### The antagonistic conformation of the USP-LBD

The AF-2 domain in the structure of the USP-LBD exhibits an antagonistic conformation generated by the ligands in the ligand-binding pocket. H12 assumes the same conformation which has been found in the case of other antagonist-bound nuclear receptors such as RXRα/oleic acid, RARα/BMS614 and ER. In all these cases, it is observed that the groove in which H12 is positioned corresponds to the binding site for the helical nuclear receptor box of nuclear receptor coactivators. This helical nuclear receptor box is distinguished by the consensus sequence LXXLL, as has been shown for the ligand-binding domain of PPAR $\gamma$ , TR $\beta$  and ER $\alpha$ . In the case of the Heliothis virescens USP, Ile-450, Ala-453 and Leu-454 of H12 are approximately in the same position as the first, second and third leucin residue of the LXXLL binding motif (IXXAL instead of LXXLL). As in other antagonistic conformations of nuclear receptors, H12 is packed into a groove of residues of H3 and H4 and of L3-4 (Val-261, Arg-265, Met-275, Glu-276, Ile-279, Ile-282, Lys-283). However, in the case of the USP-LBD, L1-3 is also involved in the groove entopology and, with the residues Phe-227, Gln-228 and Phe-229, has van-der-Waals contacts with H12.

The length of H12 in the USP-LBD is identical to that of H12 in the antagonistbound form of the RXRα-LBD. However, the structural principle which has been observed in another case of an antagonistic conformation of a nuclear receptor ligandbinding pocket is not found in its entirety in the case of the USP-LBD. Indeed, it has been found there that H11 coils up and thus permits H12 to bind to the binding groove of the nuclear receptor coactivator binding motif LXXLL. H11 is located in the extension of H10 and superposes very readily with H11 in the holo-RXRα-LBD structure, with the exception that the H11 of the USP-LBD is shorter by two residues. This is followed by a region 6 residues in length which connects H11 and H12 (His-439 to Thr-444). These amino acids of loop L11-12 span, in an extended conformation, a strand 12 Å in length. The C terminus of H11 contains three phenylalanins which are also found in RXRα. In apo-RXRα, the first two phenylalanins point towards the hydrophobic ligand-binding pocket while the third phenylalanin faces the solvent. In the agonist-bound form, the phenylalanins swap roles. In the USP-LBD, the situation is similar to the agonist-bound form of the RXRα-LBD: Phe-436 and Phe-437 face the solvent, while Phe-438 contributes to the ligandbinding pocket. In comparison with its counterpart in RXRa, the side chain of Phe-438 is rotated slightly and touches the ligand at the level of its shorter fatty acid. In the antagonist-bound form of RXRa, the first residue of the phenylalanin triplet corresponds to the end of H11. This residue is in approximately the position of the Ca atom of Phe-437. In the ligand-binding pocket, the two other phenylalanin residues, which are already part of L11-12, are orientated inwardly towards the inside of the protein. In a superposition of the Heliothis virescens USP and the antagonistbound RXRα-LBD, these two residues collide with the phospholipid ligands.

5

10

15

#### Example 6

5

10

15

20

25

30

The connecting region L1-3 interacts with H3 and L11-12 and prevents an agonistic conformation

The binding of the phospholipid in the ligand-binding pocket of the USP-LBD probably generates important structural rearrangements in the USP-LBD. The comparison with apo- and holo-RXR $\alpha$ -LBD structures allows the assumption that in the USP-LBD, too, the molecular mechanisms which bring about the ligand-bound LBD conformation comprise the displacement of H3 and H11. However, in contrast to all other nuclear receptor LBDs known to date, the structural element L1-3 plays an essential role in the Heliothis virescens USP.

Loop L1-3 interacts with H3, H11, L11-12 and H12. These structural elements are most effective by the ligand binding. L1-3 stabilizes the N-terminus of H3 via a hydrogen bridge network with Arg-243 and Asn-254 of H3. The guanidinium moiety of the Arg-243 is anchored to the backbone carbonyls of Gly-233, Ser-236 and Val-238 by strong hydrogen bridges (distances 2.61, 2.97 and 2.78 Å, respectively) and shows a van-der-Waals contact with the side chain of Val-232. In addition, the backbone amide group of the Arg-243 is bound to the carbonyl group of Pro-239 (3.20 Å) by a hydrogen bond. The side chain of Asn-254 forms hydrogen bonds with the carbonyl group of Leu-230 (2.83 Å), to the amide group of Phe-229 (3.10 Å) and, via a water molecule, to the side chain of Gln-228. Moreover, it is in van-der-Waals contact with the carbonyl group of Phe-227. The backbone carbonyl group of Asn-254 forms a strong hydrogen bridge to the side chain of Glu-226 (2.74 Å).

L1-3 (Gln-228 to Arg-231, Asp-235 and Ser-236) is also in contact with N-terminal region of H11 and with L11-12. The backbone carbonyl group of Gln-228 forms a hydrogen bond with Ala-442 (3.20 Å), and the backbone carbonyl group of Phe-229 forms a strong hydrogen bridge with the amide group of Ala-442 (2.88 Å). In addition, Arg-231 stabilizes the loop L11-12 by means of strong interactions: the

backbone amide group forms a strong hydrogen bond with the carbonyl group of Leu-440 (2.90 Å), while the side chain forms a strong hydrogen bond with the carbonyl group of His-439 (3.00 Å) and shows van-der-Waals contacts with Val-441 and Ala-442. Other interactions concern the backbone carbonyl of Asp-235 with the side chain of His-439 and a water-mediated interaction with Val-441. The hydroxyl group of Ser-236 forms a van-der-Waals contact with the side chain of Leu-440.

It is important to state that a high degree of sequence conservation exists in all residues which participate in the interaction of L1-3 with H3 and with L11-12. The main interaction partners of H3, Arg-243 and Asn-254, are conserved strictly in all lepidopteran USPs. Likewise all interaction partners in L1-3 (Glu-226, Phe-227, Gln-228, Phe-229, Leu-230, Val-232, Gly-233, Ser-236, Val-238, Pro-239) are conserved strictly in all lepidopteran USPs, with the exception of Phe-227 and Phe-229, which are replaced by leucine and isoleucine in the Bombyx mori USP. In the case of the interactions of L1-3 with L11-12, too, the residues involved (L1-3: Gln-228 to Arg-231, Asp-235 and Ser-236; L11-12: His-439 to Ala-442) are conserved strictly in all lepidopteran USPs, with the exception of Phe-229 and Asp-235. This strongly suggests that interaction patterns of L1-3 with H3 and of L1-3 with L11-12 are similar in all lepidopteran USPs.

In the superposition of Heliothis virescens USP with the holo-RXR $\alpha$ -LBDs, it can be observed that some residues from L1-3 are approximately in the same position in the Heliothis virescens USP (Asn-237, Ser-236 and Phe-229), such as residues from L11-12 of holo-RXR $\alpha$  (Asp-444, Thr-445 and Phe-450). This comparison permits the informative conclusion that L1-3 in its actual conformation excludes the existence of an agonistic conformation since this would be hindered at loop L11-12. In any case, this is no crystallization artefact and reflects the particular role of this structural element in the lepidopteran USPs.

The sterical hindering of the agonistic position of H12 here is a constitutive component of the receptor structure and not the consequence of the bulky shape of

20

25

30

5

10

the ligand, as is the case in other nuclear receptor LBDs which are occupied by fully antagonistic ligands.

It can be predicted that ligand binding of agonists generates a change in the conformation of the USP-LBD, which makes L1-3, H12 and the other LBD residues which have been described jump into an antagonistic position.

In any case, this is not a crystallization artefact and constitutes the particular role of this structural element in the lepidopteran USPs.

## Example 7

 $\frac{\text{Agonistic}}{\text{modelling, based on the RXR}\alpha/9\text{-cis-RA complex}} \quad \text{USP-LBD} \quad \text{by} \quad \text{homology}$ 

In order to gene

In order to generate a 3D model of the Heliothis virescens USP-LBD, the lacking residues of the loop between helices H1 and H3 (L1-3) were complemented from the hRXRa crystal structure in such a way that a continuous backbone is formed. The resulting structure is the experimental hRXRa reference model.

20

25

5

10

Two hRXR $\alpha$  monomers were observed in the hRXR $\alpha$  standard cell, and the L1-3 region was poorly resolved in each of these monomers. Superposition of the two structures, which had been refined independently of one another, led to a suggestion as to where this loop should be modelled. A complete 3D model of hRXR $\alpha$  based on crystal structure and in which the residues in L1-3 are completed was built. The hydrogen atoms were completed with the aid of the Hgenerate option of the Charmm program.

The L1-3 region was relaxed by Powell minimization of the Charmm program (1000 optimization steps, dielectric constant: 4, gradient tolerance: 10<sup>-6</sup>, step width 0.02, cutoff for non-binding interactions: 15 Å).

15

This optimized structure was used as template for the homology model of the Heliothis virescens USP-LBD.

5 The amino acid sequences of the Heliothis virescens USP-LBD and of hRXRα were assigned in accordance with Table 2.

With the aid of the software package Modeller and its standard settings, a 3D model was built with the aid of the assignment. The USP-LBD sequence shows a few insertions in loop 1-3 and in the loop before the first \( \beta\)-pleated sheet. In order to establish meaningful conformations for these two regions, the option lego-loop of the software package O was used. The USP model structure was subsequently subjected to Powell minimization (2000 optimization steps, dielectric constant: 4, gradient tolerance: 10<sup>-6</sup>, step width 0.02, cutoff for non-binding interactions: 15 Å). The quality of the structure thus obtained is analyzed with the program PROCHECK. Accordingly, 97% of the residues are in permitted regions and less than 2% of the residues are in prohibited regions. The latter are in the above-described modified regions.

## 20 Example 8

Comparison between the agonistic USP-LBD structure obtained from the hRXRα/9-cis RA complex and the USP-LBD crystal structure

25 The largest differences between these two structures are in the position of the activation helix (H12) and the path of the loop between the helices H1 and H3. The activation helix H12 is located in the experimental structure in the antagonistic position, while in the model structure it assumes an agonistic conformation which closes the ligand-binding niche. In the experimental structure, the loop L1-3 lies above the helix H3 and stabilizes the antagonistic position of H12 by hydrophobic contact. In contrast, this loop lies at a considerable distance from the central AFS-AD

Tobaco sassoned

5

10

15

20

helix in the agonistic homology model. Loop L1-3 is separated from helix H3 by the \(\beta\)-pleated sheet.

Moreover, the size of the ligand-binding niche differs substantially between the two structures. The presence of the large fatty acid residue in the USP-LBD crystal structure causes a great cavity by shifting helices H3, H6 and H11. In the USP agonistic conformation, these helices are packed densely and produce a smaller ligand-binding niche.

The regions of the C-terminal ends of H3, H4, H5, H8 and H9 are rigid and capable of very good superposition in the two structures. In contrast, loop L1-3 and the C-termini of H3, H6 and H11 in the two structures are displaced relative to each other. These segments form the most mobile region of the ligand-binding domain of nuclear receptors. This movement is probably specific for each receptor and the ligand-generated displacement.

### Information on the sequence listing

SEQ ID NO: 1 shows the amino acid sequence of the Heliothis virescens USP-LBD.

SEQ ID NO: 2 shows the amino acid sequence of the Heliothis virescens USP.

20

30

### Information on the Tables

Table 1 shows the structure coordinates of the LBD of the Heliothis virescens USP.

5 Table 2 shows the amino acid sequence assignment for hRXRα and USP of Heliothis virescens and of further nuclear receptor LBDs for generateing a homology model of the agonistic USP conformation.

### Table 1

10 REMARK coordinates from restrained individual B-factor refinement

REMARK refinement resolution: 20.0 - 1.65 A

REMARK starting r= 0.2151 free\_r= 0.2506

REMARK final r= 0.2112 free\_r= 0.2459

REMARK B rmsd for bonded mainchain atoms= 1.437 target= 1.5

REMARK B rmsd for bonded sidechain atoms= 2.272 target= 2.0

REMARK B rmsd for angle mainchain atoms= 2.299 target= 2.0

REMARK B rmsd for angle sidechain atoms= 3.310 target= 2.5

REMARK rweight= 0.1000 (with wa= 1.12122)
REMARK target= mlf steps= 30

REMARK sg= P4(3)22 a= 58.211 b= 58.211 c= 144.687 alpha= 90 beta= 90 gamma= 90

REMARK parameter file 1 : CNS\_TOPPAR:protein\_rep.param

REMARK parameter file 2 : CNS\_TOPPAR:water\_rep.param

REMARK parameter file 3 : eph.par

REMARK molecular structure file: alternate.mtf

25 REMARK input coordinates; anneal 2.pdb

REMARK reflection file= /home/billas/USP/SCALE0400/merge1A65/usp\_20a1a65.10.cv

REMARK ncs= none

REMARK B-correction resolution: 6.0 - 1.65

REMARK initial B-factor correction applied to fobs :

REMARK B11= -1.985 B22= -1.985 B33= 3.970 REMARK B12= 0.000 B13= 0.000 B23= 0.000

REMARK B-factor correction applied to coordinate array B: -0.193

REMARK bulk solvent: density level= 0.33501 e/A^3, B-factor= 48.7849 A^2

REMARK reflections with IFobsl/sigma F < 0.0 rejected

35 REMARK reflections with |Fobs| > 10000 \* rms(Fobs) rejected

MOTA

ATOM

25 N GLU 207 26 CA GLU 207

REMARK theoretical total number of refl. in resol. range: 30842 ( 100.0 % ) REMARK number of unobserved reflections (no entry or |F|=0): 1417 ( 4.6 % ) REMARK number of reflections rejected: 0(0.0%) 29425 ( 95.4 % ) REMARK total number of reflections used: REMARK number of reflections in working set: 26453 (85.8%) 5 2972 ( 9.6 % ) REMARK number of reflections in test set: CRYST1 58.211 58.211 144.687 90.00 90.00 90.00 P 43 2 2 REMARK FILENAME="/home/billas/LUC/13cns/bind\_2.pdb" REMARK DATE: 4-Jun-00 14:33:10 created by user: billas 10 REMARK VERSION:1.0 ATOM 1 CB ALA 203 16.114 28.799 41.997 1.00 66.21 15.029 28.899 39.746 1.00 66.49 ATOM 2 C ALA 203 14.609 30.031 39.487 1.00 66.58 3 O ALA 203 ATOM 17.364 29.707 40.068 1.00 66.33 4 N ALA 203 ATOM 16.347 28.703 40.490 1.00 66.40 15 ATOM 5 CA ALA 203 14.387 27.790 39.393 1.00 66.05 6 N ALA 204 ATOM 13,106 27.833 38.698 1.00 65.56 7 CA ALA 204 ATOM 8 CB ALA 204 12.933 26.584 37.843 1.00 65.11 MOTA 12.028 27.888 39.776 1.00 64.97 MOTA 9 C ALA 204 12.259 27.413 40.890 1.00 65.54 20 ATOM 10 O ALA 204 10.872 28.478 39.463 1.00 63.97 ATOM 11 N ALA 205 9,773 28.563 40.431 1.00 62.46 ATOM 12 CA ALA 205 8.437 28.736 39.705 1.00 62.71 13 CB ALA 205 ATOM 9.798 27.243 41.190 1.00 61.33 ATOM 14 C ALA 205 15 O ALA 205 9.426 26.199 40.647 1.00 61.43 25 **ATOM** 10.251 27.285 42.439 1.00 59.43 16 N GLN 206 ATOM 17 CA GLN 206 10.372 26.060 43.211 1.00 57.60 ATOM 11.198 26.298 44.472 1.00 58.55 18 CB GLN 206 ATOM 11.976 25.062 44.863 1.00 60.08 ATOM 19 CG GLN 206 12.831 24.542 43.712 1.00 61.69 30 20 CD GLN 206 ATOM 13.892 25.094 43.411 1.00 62.30 ATOM 21 OE1 GLN 206 12.360 23.486 43.053 1.00 61.64 22 NE2 GLN 206 ATOM 23 C GLN 206 9.072 25.355 43.567 1.00 55.19 ATOM ATOM 24 O GLN 206 8.089 25.972 43.983 1.00 55.16

9.099 24.040 43.382 1.00 52.39

7.970 23.165 43.644 1.00 49.47

Q
4
4
AUD AUD
42
U
U
m
×
1
T
C
ũ

ATOM	27 CB GLU 207	7.755 22.243 42.447 1.00 52.06
ATOM	28 CG GLU 207	6.603 21.264 42.591 1.00 55.45
ATOM	29 CD GLU 207	5.266 21.897 42.275 1.00 57.54
ATOM	30 OE1 GLU 207	4.249 21.167 42.254 1.00 58.63
ATOM	31 OE2 GLU 207	5.235 23.125 42.043 1.00 58.53
ATOM	32 C GLU 207	8.273 22.311 44.861 1.00 45.64
ATOM	33 O GLU 207	9.419 21.945 45.089 1.00 44.54
ATOM	34 N LEU 208	7.244 21.996 45.637 1.00 41.48
ATOM	35 CA LEU 208	7.408 21.142 46.810 1.00 38.35
ATOM	36 CB LEU 208	6.204 21.323 47.752 1.00 36.20
ATOM	37 CG LEU 208	6.211 20.671 49.134 1.00 34.07
ATOM	38 CD1 LEU 208	7.495 21.026 49.867 1.00 32.61
ATOM	39 CD2 LEU 208	5.003 21.158 49.926 1.00 33.18
ATOM	40 C LEU 208	7.472 19.709 46.267 1.00 38.07
ATOM	41 O LEU 208	6.443 19.122 45.919 1.00 38.80
ATOM	42 N SER 209	8.682 19.155 46.174 1.00 34.84
ATOM	43 CA SER 209	8.882 17.803 45.647 1.00 33.19
MOTA	44 CB SER 209	9.257 17.883 44.165 1.00 32.93
ATOM	45 OG SER 209	10.582 18.382 44.024 1.00 33.12
MOTA	46 C SER 209	10.005 17.062 46.393 1.00 32.84
MOTA	47 O SER 209	10.824 17.685 47.057 1.00 32.20
ATOM	48 N ILE 210 1	10.048 15.736 46.261 1.00 32.33
ATOM	49 CA ILE 210	11.092 14.945 46.917 1.00 34.10
ATOM	50 CB ILE 210	10.961 13.438 46.613 1.00 35.86
ATOM	51 CG2 ILE 210	12.017 12.667 47.387 1.00 37.65
ATOM	52 CG1 ILE 210	9.565 12.929 46.980 1.00 36.30
ATOM	53 CD1 ILE 210	9.239 13.004 48.447 1.00 35.19
ATOM	54 C ILE 210	12.478 15.370 46.436 1.00 33.53
ATOM	55 O ILE 210	13.420 15.467 47.225 1.00 30.63
ATOM	56 N GLU 211	12.607 15.609 45.136 1.00 33.07
ATOM	57 CA GLU 211	13.898 16.012 44.587 1.00 33.86
ATOM	58 CB GLU 211	13.797 16.199 43.066 1.00 36.35
MOTA	59 CG GLU 211	15.042 16.838 42.436 1.00 40.50
ATOM	60 CD GLU 211	14.880 17.104 40.941 1.00 43.91
ATOM	61 OE1 GLU 211	15.777 17.748 40.348 1.00 45.56
ATOM	62 OE2 GLU 211	13.857 16.667 40.365 1.00 44.68

10

15

20

25

30

35

63 C GLU 211 14.396 17.299 45.246 1.00 32.93 ATOM 15.552 17.395 45.637 1.00 32.96 64 O GLU 211 ATOM 13.524 18.292 45.365 1.00 31.58 ATOM 65 N ARG 212 13.914 19.545 45.994 1.00 30.93 66 CA ARG 212 ATOM 67 CB ARG 212 12,799 20,579 45,850 1,00 31,30 ATOM 13.111 21.897 46.547 1.00 34.79 ATOM 68 CG ARG 212 69 CD ARG 212 14.482 22.417 46.130 1.00 36.82 ATOM 14.880 23.599 46.886 1.00 40.98 70 NE ARG 212 ATOM 71 CZ ARG 212 16.109 24.103 46.876 1.00 41.42 ATOM 17.055 23.527 46.148 1.00 43.03 72 NH1 ARG 212 ATOM ATOM 73 NH2 ARG 212 16,395 25,178 47,596 1,00 43,71 14.277 19.375 47.478 1.00 29.92 ATOM 74 C ARG 212 15.218 20.000 47.970 1.00 30.04 ATOM 75 O ARG 212 76 N LEU 213 13.529 18.541 48.195 1.00 28.52 ATOM 77 CA LEU 213 13.819 18.322 49.612 1.00 27.44 ATOM 12.711 17.471 50.272 1.00 25.96 ATOM 78 CB LEU 213 79 CG LEU 213 11,361 18,184 50,410 1,00 27,73 **ATOM** 80 CD1 LEU 213 10.306 17.200 50.892 1.00 24.70 ATOM 81 CD2 LEU 213 11.492 19.344 51.358 1.00 27.22 ATOM ATOM 82 C LEU 213 15.172 17.625 49.757 1.00 27.41 15.895 17.861 50.722 1.00 27.85 **MOTA** 83 O LEU 213 15.510 16.761 48.802 1.00 28.81 ATOM 84 N LEU 214 16.792 16.068 48.874 1.00 30.82 85 CA LEU 214 **ATOM** 16.863 14.926 47.851 1.00 29.94 86 CB LEU 214 ATOM 16.112 13.655 48.272 1.00 30.12 ATOM 87 CG LEU 214 16.047 12.663 47.117 1.00 30.68 ATOM 88 CD1 LEU 214 ATOM 89 CD2 LEU 214 16.820 13.015 49.467 1.00 31.09 90 C LEU 214 17.914 17.067 48.646 1.00 33.09 ATOM 18.954 16.985 49.297 1.00 32.71 ATOM 91 O LEU 214 17.700 18.018 47.736 1.00 35.01 ATOM 92 N GLU 215 18,702 19,046 47,471 1,00 36,86 **ATOM** 93 CA GLU 215 18.274 19.977 46.319 1.00 38.74 94 CB GLU 215 **ATOM** 95 CG GLU 215 18.045 19.310 44.962 1.00 42.50 ATOM 17.655 20.307 43.862 1.00 44.43 **ATOM** 96 CD GLU 215 17.034 21.350 44.174 1.00 44.44 ATOM 97 OE1 GLU 215 98 OE2 GLU 215 17.957 20.039 42.674 1.00 46.05 ATOM

10

15

20

25

30

35

18.881 19.886 48.735 1.00 36.72 ATOM 99 C GLU 215 19.996 20.278 49.082 1.00 37.76 ATOM 100 O GLU 215 17.779 20.159 49.430 1.00 35.08 ATOM 101 N MET 216 17.814 20.970 50.644 1.00 34.20 ATOM 102 CA MET 216 16.393 21.402 51.018 1.00 32.09 103 CB MET 216 ATOM 104 CG MET 216 15.820 22.514 50.188 1.00 31.14 ATOM 14.067 22.656 50.591 1.00 29.63 ATOM 105 SD MET 216 106 CE MET 216 14.187 23.383 52.223 1.00 30.33 ATOM 18.447 20.309 51.868 1.00 33.78 ATOM 107 C MET 216 108 O MET 216 18.955 20.998 52.755 1.00 32.43 ATOM 109 N GLU 217 18.381 18.982 51.923 1.00 34.02 ATOM 110 CA GLU 217 18.908 18.212 53.046 1.00 35.35 ATOM 18.470 16.745 52.919 1.00 33.44 111 CB GLU 217 ATOM 18.729 15.871 54.148 1.00 32.91 ATOM 112 CG GLU 217 113 CD GLU 217 17.999 16.372 55.389 1.00 32.03 ATOM 17.001 17.104 55.242 1.00 33.02 114 OE1 GLU 217 ATOM 18.419 16.032 56.511 1.00 34.58 ATOM 115 OE2 GLU 217 20.421 18.293 53.105 1.00 37.01 116 C GLU 217 **ATOM** ATOM 117 O GLU 217 21,006 18,276 54,190 1.00 37.08 118 N SER 218 21.036 18.406 51.928 1.00 39.66 ATOM 22.491 18.476 51.795 1.00 42.68 ATOM 119 CA SER 218 120 CB SER 218 22.913 18.001 50.408 1.00 43.25 **ATOM** 121 OG SER 218 22.571 16.640 50.214 1.00 46.19 ATOM ATOM 122 C SER 218 23.083 19.856 52.027 1.00 44.17 24.250 19.978 52.395 1.00 43.66 ATOM 123 O SER 218 22.291 20.895 51.797 1.00 46.04 ATOM 124 N LEU 219 22.773 22.254 51.982 1.00 48.34 ATOM 125 CA LEU 219 ATOM 126 CB LEU 219 21.706 23.265 51.556 1.00 49.36 ATOM 127 CG LEU 219 21.670 23.631 50.072 1.00 50.71 21,879 22,395 49,219 1.00 51.07 ATOM 128 CD1 LEU 219 129 CD2 LEU 219 20.341 24.307 49.760 1.00 51.61 ATOM 130 C LEU 219 23.183 22.530 53.416 1.00 49.65 ATOM ATOM 131 O LEU 219 22.501 22.140 54.363 1.00 49.02 24.318 23.205 53.552 1.00 51.55 132 N VAL 220 ATOM ATOM 133 CA VAL 220 24.868 23.592 54.843 1.00 53.29 134 CB VAL 220 26.250 22.945 55.085 1.00 52.35 ATOM

440
40
4
100
4
10
15
Ch
16
Tree.
3
T.
(mor
(*)
4 .

ATOM	135 CG1 VAL 220	26.774 23.341 56.456 1.00 51.60
ATOM	136 CG2 VAL 220	26.142 21.426 54.965 1.00 50.84
ATOM	137 C VAL 220	25.030 25.106 54.770 1.00 55.56
ATOM	138 O VAL 220	25.929 25.613 54.097 1.00 56.16
ATOM	139 N ALA 221	24.147 25.823 55.450 1.00 57.83
ATOM	140 CA ALA 221	24.190 27.278 55.428 1.00 60.51
ATOM	141 CB ALA 221	22.782 27.845 55.601 1.00 60.73
ATOM	142 C ALA 221	25.108 27.838 56.499 1.00 61.87
ATOM	143 O ALA 221	25.475 27.143 57.452 1.00 62.13
ATOM	144 N ALA 222	25.490 29.100 56.326 1.00 62.85
ATOM	145 CA ALA 222	26.345 29.756 57.295 1.00 63.37
ATOM	146 CB ALA 222	26.612 31.196 56.871 1.00 63.59
ATOM	147 C ALA 222	25.564 29.719 58.601 1.00 63.51
ATOM	148 O ALA 222	24.422 30.176 58.659 1.00 63.95
ATOM	149 N ALA 223	26.173 29.150 59.636 1.00 63.63
ATOM	150 CA ALA 223	25.532 29.044 60.939 1.00 63.10
ATOM	151 CB ALA 223	26.558 28.627 61.984 1.00 63.64
ATOM	152 C ALA 223	24.874 30.365 61.339 1.00 62.58
ATOM	153 O ALA 223	25.557 31.333 61.678 1.00 63.33
ATOM	154 N ALA 224	23.544 30.399 61.290 1.00 61.31
ATOM	155 CA ALA 224	22.789 31.599 61.644 1.00 59.25
ATOM	156 CB ALA 224	21.323 31.440 61.220 1.00 58.51
ATOM	157 C ALA 224	22.878 31.880 63.143 1.00 58.07
ATOM	158 O ALA 224	22.988 30.943 63.939 1.00 58.18
ATOM	159 N GLU 225	22.844 33.159 63.528 1.00 56.07
ATOM	160 CA GLU 225	22.909 33.507 64.950 1.00 54.05
ATOM	161 CB GLU 225	22.498 34.969 65.221 1.00 54.53
ATOM	162 CG GLU 225	22.700 35.401 66.703 1.00 55.83
ATOM	163 CD GLU 225	21.439 35.872 67.407 1.00 56.62
ATOM	164 OE1 GLU 225	21.407 35.822 68.663 1.00 57.35
ATOM	165 OE2 GLU 225	20.464 36.314 66.743 1.00 57.42
ATOM	166 C GLU 225	21.901 32.594 65.611 1.00 52.71
ATOM	167 O GLU 225	20.737 32.557 65.201 1.00 52.66
ATOM	168 N GLU 226	22.334 31.840 66.612 1.00 50.26
ATOM	169 CA GLU 226	21.391 30.960 67.256 1.00 47.92
ATOM	170 CB GLU 226	21.858 29.513 67.196 1.00 49.61

_	F. Frida
	1
	V.
	1000
	1
	U.S
	UF
	it
	3
	ñ,

ATOM	171 CG GLU 226	20.778 28.525 67.641 1.00 49.78
ATOM	172 CD GLU 226	19.333 28.959 67.359 1.00 51.91
ATOM	173 OE1 GLU 226	18.452 28.312 67.956 1.00 50.08
ATOM	174 OE2 GLU 226	19.039 29.909 66.543 1.00 51.77
ATOM	175 C GLU 226	21.015 31.344 68.670 1.00 46.28
ATOM	176 O GLU 226	21.839 31.794 69.476 1.00 47.17
ATOM	177 N PHE 227	19.733 31.155 68.942 1.00 41.52
ATOM	178 CA PHE 227	19.138 31.503 70.206 1.00 38.73
ATOM	179 CB PHE 227	17.723 32.022 69.963 1.00 40.03
ATOM	180 CG PHE 227	17.640 33.061 68.876 1.00 40.91
MOTA	181 CD1 PHE 227	17.775 32.703 67.542 1.00 40.72
ATOM	182 CD2 PHE 227	17.464 34.402 69.192 1.00 42.62
ATOM	183 CE1 PHE 227	17.739 33.661 66.535 1.00 42.04
ATOM	184 CE2 PHE 227	17.426 35.374 68.188 1.00 42.27
ATOM	185 CZ PHE 227	17.564 34.996 66.857 1.00 42.02
ATOM	186 C PHE 227	19.119 30.339 71.174 1.00 34.83
ATOM	187 O PHE 227	19.218 29.178 70.778 1.00 34.52
ATOM	188 N GLN 228	18.982 30.687 72.445 1.00 33.69
ATOM	189 CA GLN 228	18.979 29.735 73.540 1.00 32.01
ATOM	190 CB GLN 228	19.290 30.468 74.847 1.00 34.80
ATOM	191 CG GLN 228	20.680 31.080 74.935 1.00 39.39
ATOM	192 CD GLN 228	21.768 30.029 74.916 1.00 40.63
ATOM	193 OE1 GLN 228	22.117 29.504 73.860 1.00 44.27
ATOM	194 NE2 GLN 228	22.301 29.706 76.093 1.00 42.65
ATOM	195 C GLN 228	17.678 28.974 73.736 1.00 28.92
ATOM	196 O GLN 228	17.035 29.174 74.750 1.00 28.29
ATOM	197 N PHE 229	17.283 28.120 72.794 1.00 28.04
ATOM	198 CA PHE 229	16.056 27.340 72.996 1.00 25.30
ATOM	199 CB PHE 229	15.767 26.411 71.821 1.00 27.02
ATOM	200 CG PHE 229	15.066 27.055 70.680 1.00 28.71
ATOM	201 CD1 PHE 229	15.599 28.170 70.052 1.00 28.96
ATOM	202 CD2 PHE 229	13.903 26.480 70.173 1.00 30.61
ATOM	203 CE1 PHE 229	14.991 28.708 68.918 1.00 29.32
ATOM	204 CE2 PHE 229	13.284 26.998 69.046 1.00 31.44
ATOM	205 CZ PHE 229	13.829 28.117 68.412 1.00 31.43
MOTA	206 C PHE 229	16.276 26.434 74.195 1.00 23.81

_	00	5
	Sept S	-
	No.	
	1	
	A.	2
	100	-
	CA CHE STATE OF STATES	-
	2	1
	7	
	C	
	4	Ser.
	Ed A Mil	-
	F 8 F 8	
	10	1
	1.	ć

ATOM 2	207 O PHE 229 15.385 26.202 75.014 1.00	22.15
ATOM 2	208 N LEU 230 17.487 25.899 74.263 1.00	20.44
ATOM 2	209 CA LEU 230 17.848 24.964 75.302 1.0	0 21.42
ATOM 2	210 CB LEU 230 18.255 23.631 74.650 1.0	0 20.34
ATOM 2	211 CG LEU 230 17.191 22.855 73.834 1.0	0 22.70
ATOM 2	212 CD1 LEU 230 17.860 21.762 73.013 1.	00 23.14
ATOM 2	213 CD2 LEU 230 16.130 22.252 74.773 1.	00 21.55
ATOM 2	214 C LEU 230 19.017 25.540 76.094 1.00	20.71
ATOM 2	215 O LEU 230 19.977 26.038 75.524 1.00	20.61
ATOM 2	216 N ARG 231 18.931 25.467 77.411 1.0	0 20.48
ATOM :	217 CA ARG 231 20.018 25.997 78.211 1.6	00 20.62
ATOM	218 CB ARG 231 20.023 27.525 78.176 1.	00 20.50
ATOM	219 CG ARG 231 18.907 28.184 79.017 1.	00 24.52
ATOM	220 CD ARG 231 17.560 28.025 78.342 1.	00 27.62
ATOM	221 NE ARG 231 16.465 28.674 79.060 1.	00 28.14
ATOM	222 CZ ARG 231 15.846 28.165 80.118 1.	00 28.35
ATOM	223 NH1 ARG 231 16.208 26.986 80.598 1	.00 27.27
ATOM	224 NH2 ARG 231 14.856 28.835 80.692 1	.00 28.94
ATOM	225 C ARG 231 19.957 25.585 79.663 1.0	0 20.62
ATOM	226 O ARG 231 18.884 25.350 80.219 1.0	00 20.08
ATOM	227 N VAL 232 21.138 25.549 80.265 1.0	0 20.70
ATOM	228 CA VAL 232 21.276 25.244 81.684 1.0	00 23.23
ATOM	229 CB VAL 232 22.596 24.499 81.961 1.0	
ATOM	230 CG1 VAL 232 22.800 24.335 83.460 1	.00 24.88
ATOM	231 CG2 VAL 232 22.565 23.135 81.289 1	.00 23.34
ATOM	232 C VAL 232 21.306 26.619 82.359 1.0	
ATOM	233 O VAL 232 22.284 27.349 82.225 1.0	0 29.87
ATOM	234 N GLY 233 20.232 26.960 83.062 1.0	
ATOM	235 CA GLY 233 20.137 28.249 83.730 1.	
ATOM	236 C GLY 233 20.170 28.129 85.240 1.0	
ATOM	237 O GLY 233 20.449 27.041 85.755 1.0	
ATOM	238 N PRO 234 19.863 29.206 85.980 1.	
ATOM	239 CD PRO 234 19.340 30.507 85.515 1	
ATOM	240 CA PRO 234 19.886 29.158 87.447 1	
ATOM	241 CB PRO 234 19.772 30.627 87.833 1	
ATOM	242 CG PRO 234 18.804 31.123 86.802 1	.00 32.04

	ATOM	243 C PRO 234 18.752 28.323 88.037 1.00 27.91	
	ATOM	244 O PRO 234 18.781 27.975 89.229 1.00 28.03	
	ATOM	245 N ASP 235 17.757 27.996 87.210 1.00 26.13	
	ATOM	246 CA ASP 235 16.636 27.186 87.680 1.00 23.93	
5	ATOM	247 CB ASP 235 15.333 27.686 87.064 1.00 28.77	
	ATOM	248 CG ASP 235 15.405 27.820 85.544 1.00 31.24	
	ATOM	249 OD1 ASP 235 16.519 27.836 84.964 1.00 32.56	
	ATOM	250 OD2 ASP 235 14.327 27.922 84.919 1.00 34.70	
	ATOM	251 C ASP 235 16.828 25.700 87.362 1.00 20.99	
10	ATOM	252 O ASP 235 16.019 24.881 87.751 1.00 19.94	
	ATOM	253 N SER 236 17.914 25.369 86.666 0.50 20.63	AC1
	ATOM	254 CA SER 236 18.208 23.979 86.280 0.50 20.15	AC1
	ATOM	255 CB SER 236 19.196 23.969 85.111 0.50 19.44	AC1
	ATOM	256 OG SER 236 18.708 24.734 84.013 0.50 19.16	AC1
15	ATOM	257 C SER 236 18.787 23.137 87.425 0.50 21.81	AC1
	ATOM	258 O SER 236 19.849 23.457 87.946 0.50 20.58	AC1
	ATOM	259 N ASN 237 18.125 22.037 87.782 1.00 21.94	
	ATOM	260 CA ASN 237 18.621 21.202 88.886 1.00 25.34	
	ATOM	261 CB ASN 237 17.498 20.331 89.450 1.00 30.84	
20	ATOM	262 CG ASN 237 17.020 19.301 88.472 1.00 34.04	
	ATOM	263 OD1 ASN 237 17.786 18.838 87.623 1.00 39.37	
	ATOM	264 ND2 ASN 237 15.748 18.913 88.588 1.00 39.05	
	ATOM	265 C ASN 237 19.843 20.325 88.581 1.00 26.93	
	ATOM	266 O ASN 237 20.180 19.405 89.339 1.00 32.05	
25	ATOM	267 N VAL 238 20.537 20.621 87.503 1.00 23.03	
	ATOM	268 CA VAL 238 21.713 19.862 87.114 1.00 20.81	
	ATOM	269 CB VAL 238 22.096 20.241 85.663 1.00 20.25	
	ATOM	270 CG1 VAL 238 23.336 19.495 85.207 1.00 19.20	
	ATOM	271 CG2 VAL 238 20.919 19.922 84.741 1.00 20.14	
30	ATOM	272 C VAL 238 22.844 20.185 88.106 1.00 20.62	
	ATOM	273 O VAL 238 23.147 21.343 88.363 1.00 18.94	
	ATOM	274 N PRO 239 23.428 19.153 88.719 1.00 20.32	
	ATOM	275 CD PRO 239 23.144 17.726 88.541 1.00 20.40	
	ATOM	276 CA PRO 239 24.515 19.328 89.688 1.00 21.49	
35	ATOM	277 CB PRO 239 24.911 17.892 90.023 1.00 22.13	
	ATOM	278 CG PRO 239 23.696 17.174 89.847 1.00 20.51	

10

15

20

25

30

35

ATOM 279 C PRO 239 25.663 20.039 89.023 1.00 24.59 ATOM 280 O PRO 239 25.924 19.804 87.847 1.00 23.65 ATOM 281 N PRO 240 26.388 20.879 89.777 1.00 24.92 ATOM 282 CD PRO 240 26.142 21.311 91.167 1.00 26.02 ATOM 283 CA PRO 240 27.524 21.603 89.202 1.00 26.88 ATOM 284 CB PRO 240 28.222 22.161 90.438 1.00 26.73 27.039 22.543 91.299 1.00 29.18 ATOM 285 CG PRO 240 ATOM 286 C PRO 240 28.434 20.733 88.363 1.00 26.35 ATOM 287 O PRO 240 28.847 21.125 87.259 1.00 27.72 ATOM 288 N LYS 241 28.745 19.533 88.838 1.00 28.50 ATOM 289 CA LYS 241 29.642 18.682 88.071 1.00 28.19 ATOM 290 CB LYS 241 30.073 17.457 88.878 1.00 32.48 ATOM 291 CG LYS 241 28,970 16,508 89,292 1,00 34,64 ATOM 292 CD LYS 241 29.627 15.241 89.832 1.00 37.47 ATOM 293 CE LYS 241 28.627 14.162 90.157 1.00 39.69 ATOM 294 NZ LYS 241 29.359 12.932 90.578 1.00 42.50 ATOM 295 C LYS 241 29.144 18.233 86.700 1.00 27.86 ATOM 296 O LYS 241 29.935 17.790 85.868 1.00 27.57 297 N PHE 242 ATOM 27.840 18.335 86.459 1.00 25.10 ATOM 298 CA PHE 242 27 309 17 953 85 154 1 00 22 57 ATOM 299 CB PHE 242 26.161 16.954 85.319 1.00 24.91 ATOM 300 CG PHE 242 26.600 15.619 85.856 1.00 28.41 ATOM 301 CD1 PHE 242 27.411 14.790 85.102 1.00 30.20 26.194 15.191 87.108 1.00 28.96 ATOM 302 CD2 PHE 242 ATOM 303 CE1 PHE 242 27.813 13.544 85.583 1.00 31.58 ATOM 304 CE2 PHE 242 26.594 13.943 87.596 1.00 30.20 ATOM 305 CZ PHE 242 27.400 13.127 86.832 1.00 32.03 ATOM 306 C PHE 242 26.837 19.151 84.330 1.00 19.63 ATOM 307 O PHE 242 26.386 18.991 83.190 1.00 20.79 ATOM 308 N ARG 243 26.971 20.350 84.873 1.00 19.69 MOTA 309 CA ARG 243 26.513 21.529 84.153 1.00 20.41 ATOM 310 CB ARG 243 26.538 22.749 85.066 1.00 20.87 ATOM 311 CG ARG 243 25.523 22.602 86.208 1.00 23.08 ATOM 312 CD ARG 243 25.562 23.759 87.130 1.00 26.38 MOTA 313 NE ARG 243 24.725 24.856 86.687 1.00 27.91 ATOM 314 CZ ARG 243 23.394 24.873 86.728 1.00 28.35

ATOM	315 NH1 ARG 243	22.697 23.825 87.192 1.00 26.91	
ATOM		22.764 25.975 86.343 1.00 28.11	
ATOM	317 C ARG 243	27.238 21.813 82.846 1.00 20.13	
ATOM	318 O ARG 243	26.596 22.114 81.836 1.00 19.71	
ATOM	319 N ALA 244	28.564 21.734 82.838 1.00 20.90	
ATOM	320 CA ALA 244	29.273 21.974 81.577 1.00 22.06	
ATOM	321 CB ALA 244	30.773 21.896 81.796 1.00 21.20	
ATOM	322 C ALA 244	28.842 20.984 80.492 1.00 21.05	
ATOM	323 O ALA 244	28.527 21.365 79.366 1.00 21.57	
ATOM	324 N PRO 245	28.783 19.696 80.822 1.00 21.63	
ATOM	325 CD PRO 245	29.335 19.087 82.049 1.00 25.65	
ATOM	326 CA PRO 245	28.377 18.672 79.861 1.00 22.28	
ATOM	327 CB PRO 245	28.516 17.380 80.666 1.00 24.91	
ATOM	328 CG PRO 245	29.614 17.694 81.605 1.00 25.26	
ATOM	329 C PRO 245	26.943 18.859 79.329 1.00 19.49	
ATOM	330 O PRO 245	26.691 18.778 78.118 1.00 21.31	
ATOM	331 N VAL 246	26.013 19.123 80.230 1.00 20.18	
ATOM	332 CA VAL 246	24.624 19.294 79.805 1.00 18.44	
ATOM	333 CB VAL 246	23.693 19.269 81.028 1.00 18.35	
ATOM	334 CG1 VAL 246	22.221 19.536 80.620 1.00 18.11	
ATOM	335 CG2 VAL 246		
ATOM	336 C VAL 246	24.501 20.568 78.968 1.00 18.23	
ATOM	337 O VAL 246	23.773 20.603 77.977 1.00 18.23	
ATOM	338 N SER 247	20.201 21.000 70.001 1101 2111	AC1
ATOM		25.198 22.858 78.599 0.50 21.19	AC1
ATOM	340 CB SER 247	26.058 23.910 79.289 0.50 21.37	
ATOM	341 OG SER 247		AC1
ATOM	342 C SER 247	25.712 22.621 77.189 0.50 21.32	AC1
ATOM	343 O SER 247	25.180 23.161 76.217 0.50 21.62	AC1
ATOM	344 N SER 248		
ATOM			
ATOM	346 CB SER 248	28.541 20.594 75.916 1.00 24.31	
ATOM			
ATOM	348 C SER 248		
ATOM	349 O SER 248		
ATOM	350 N LEU 249	25.513 19.895 75.519 1.00 22.35	

ATOM 351 CA LEU 249 24.462 19.185 74.791 1.00 22.28 ATOM 352 CB LEU 249 23.904 18.046 75.668 1.00 22.23 24.970 16.972 75.954 1.00 25.52 ATOM 353 CG LEU 249 ATOM 354 CD1 LEU 249 24,441 15,919 76,922 1,00 26,39 5 ATOM 355 CD2 LEU 249 25.398 16.341 74.643 1.00 27.01 ATOM 356 C LEU 249 23.358 20.152 74.352 1.00 21.63 ATOM 357 O LEU 249 22.822 20.039 73.231 1.00 19.99 ATOM 358 N CYS 250 23.012 21.102 75.217 1.00.21 10 ATOM 359 CA CYS 250 21.995 22.098 74.856 1.00 21.22 10 ATOM 360 CB CYS 250 21 701 23 044 76 019 1 00 20 65 ATOM 361 SG CYS 250 20.853 22.249 77.396 1.00 22.08 ATOM 362 C CYS 250 22.471 22.932 73.684 1.00 22.49 ATOM 363 O CYS 250 21.687 23.302 72.828 1.00 23.08 ATOM 364 N GIN 251 23 765 23 239 73 656 1 00 22 61 15 ATOM 365 CA GLN 251 24 313 24 064 72 577 1 00 24 50 ATOM 366 CB GLN 251 25.738 24.482 72.925 1.00 26.13 ATOM 367 CG GLN 251 25.827 25.428 74.123 1.00 31.89 ATOM 368 CD GLN 251 27.270 25.602 74.609 1.00 36.32 ATOM 369 OE1 GLN 251 28 146 26 020 73 846 1 00 38 70 20 ATOM 370 NE2 GLN 251 27.520 25.275 75.883 1.00 36.33 ATOM 371 C GLN 251 24,290 23,309 71,255 1,00 23,96 ATOM 372 O GLN 251 24.080 23.899 70.200 1.00 25.04 ATOM 373 N ILE 252 24.506 21.998 71.323 1.00 23.74 ATOM 374 CA ILE 252 24.475 21.143 70.140 1.00 24.05 2.5 ATOM 375 CB ILE 252 24.877 19.690 70.493 1.00 25.71 ATOM 376 CG2 ILE 252 24.385 18.727 69.419 1.00 25.12 ATOM 377 CG1 ILE 252 26.405 19.596 70.658 1.00 26.17 ATOM 378 CD1 ILE 252 26.874 18.335 71.359 1.00 27.45 ATOM 379 C ILE 252 23.032 21.183 69.642 1.00 25.30 30 ATOM 380 O ILE 252 22,760 21,312 68,448 1,00 25.88 ATOM 381 N GLY 253 22,101 21,105 70,580 1,00 25,76 ATOM 382 CA GLY 253 20.698 21.167 70.213 1.00 24.72 ATOM 383 C GLY 253 20.327 22.497 69.573 1.00 24.98 ATOM 384 O GLY 253 19.611 22.527 68.561 1.00 24.56 35 ATOM 385 N ASN 254 20.779 23.600 70.165 1.00 23.66 ATOM 386 CA ASN 254 20.483 24.929 69.642 1.00 24.18

ATOM 387 CB ASN 254 21.063 25.999 70.566 1.00 23.04 ATOM 388 CG ASN 254 20.336 26.061 71.884 1.00 24.90 ATOM 389 OD1 ASN 254 19.147 25.729 71.954 1.00 22.87 ATOM 390 ND2 ASN 254 21.020 26.511 72.934 1.00 25.39 391 C ASN 254 20.990 25.142 68.215 1.00 25.59 5 ATOM ATOM 392 O ASN 254 20.349 25.832 67.418 1.00 25.49 22.154 24.575 67.915 1.00 24.87 ATOM 393 N LYS 255 ATOM 394 CA LYS 255 22,718 24.669 66.572 1.00 26.12 ATOM 395 CB LYS 255 24.121 24.061 66.518 1.00 29.40 10 ATOM 396 CG LYS 255 25.162 24.983 67.112 1.00 33.68 ATOM 397 CD LYS 255 26.481 24.293 67.392 1.00 34.86 ATOM 398 CE LYS 255 27.280 24.027 66.150 1.00 35.57 ATOM 399 NZ LYS 255 28.719 23.853 66.527 1.00 33.75 ATOM 400 C LYS 255 21.816 23.924 65.608 1.00 26.04 15 ATOM 401 O LYS 255 21.539 24.415 64.507 1.00 25.57 ATOM 402 N GLN 256 21.358 22.741 66.009 1.00 24.02 ATOM 403 CA GLN 256 20.498 21.967 65.121 1.00 23.89 ATOM 404 CB GLN 256 20.325 20.546 65.658 1.00 25.47 ATOM 405 CG GLN 256 21.676 19.880 65.887 1.00 28.63 20 ATOM 406 CD GLN 256 21.565 18.517 66.534 1.00 30.93 ATOM 407 OE1 GLN 256 20.710 18.301 67.387 1.00 32.63 ATOM 408 NE2 GLN 256 22.439 17.599 66.149 1.00 30.18 ATOM 409 C GLN 256 19.156 22.658 64.915 1.00 24.45 ATOM 410 O GLN 256 18.596 22.598 63.828 1.00 24.20 25 ATOM 411 N HF 257 18.662 23.338 65.942 1.00.23.21 ATOM 412 CA ILE 257 17.390 24.059 65.816 1.00 22.41 ATOM 413 CB ILE 257 16.895 24.535 67.180 1.00 20.26 ATOM 414 CG2 ILE 257 15.636 25.401 67.021 1.00 21.15 ATOM 415 CG1 ILE 257 16.607 23.298 68.039 1.00 22.12 30 ATOM 416 CD1 ILE 257 16.309 23.620 69.517 1.00 21.36 ATOM 417 C ILE 257 17.558 25.253 64.877 1.00 23.91 ATOM 418 O ILE 257 16.677 25.544 64.060 1.00 21.49 ATOM 419 N ALA 258 18.684 25.949 64.994 1.00 23.86 ATOM 420 CA ALA 258 18.939 27.081 64.103 1.00 25.37 35 ATOM 421 CB ALA 258 20.313 27.705 64.416 1.00 26.26 ATOM 422 C ALA 258 18,906 26,588 62,656 1,00 25,01

10

15

20

2.5

30

35

ATOM 423 O ALA 258 18.306 27.238 61.783 1.00 25.91 ATOM 424 N ALA 259 19.555 25.450 62.403 1.00 23.72 ATOM 425 CA ALA 259 19.602 24.865 61.063 1.00 24.51 ATOM 426 CB ALA 259 20.442 23.613 61.058 1.00 24.62 ATOM 427 C ALA 259 18 187 24 525 60 623 1 00 24 36 ATOM 428 O ALA 259 17.846 24.693 59.464 1.00 23.27 ATOM 429 N LEU 260 17.374 24.015 61.544 1.00 23.02 ATOM 430 CA LEU 260 15.986 23.685 61.188 1.00 24.75 ATOM 431 CB LEU 260 15.237 23.070 62.366 1.00 26.22 ATOM 432 CG LEU 260 15 550 21 633 62 742 1 00 31 27 ATOM 433 CD1 LEU 260 14.906 21.342 64.082 1.00 32.20 ATOM 434 CD2 LEU 260 15.054 20.679 61.658 1.00 33.32 ATOM 435 C LEU 260 15.214 24.902 60.750 1.00 25.40 ATOM 436 O LEU 260 14.391 24.821 59.834 1.00 23.40 ATOM 437 N VAL 261 15.439 26.031 61.419 1.00 25.21 ATOM 438 CA VAL 261 14.735 27.247 61.055 1.00 26.95 ATOM 439 CB VAL 261 15.050 28.411 62.036 1.00 25.46 ATOM 440 CG1 VAL 261 14.386 29.700 61.544 1.00 27.40 ATOM 441 CG2 VAL 261 14.520 28.075 63.434 1.00 27.42 ATOM 442 C VAL 261 15.104 27.671 59.640 1.00 26.53 ATOM 443 O VAL 261 14.232 28.035 58.850 1.00 25.34 ATOM 444 N VAL 262 16.396 27.611 59.320 1.00 27.29 ATOM 445 CA VAL 262 16.874 27.995 57.993 1.00 28.11 ATOM 446 CB VAL 262 18.430 27.910 57.905 1.00 30.08 ATOM 447 CG1 VAI 262 18 883 27 872 56 441 1 00 33 75 ATOM 448 CG2 VAL 262 19.051 29.104 58.606 1.00 32.97 ATOM 449 C VAL 262 16.267 27.075 56.939 1.00 26.73 ATOM 450 O VAL 262 15.909 27.511 55.840 1.00 26.28 ATOM 451 N TRP 263 16.177 25.794 57.286 1.00 24.38 ATOM 452 CA TRP 263 15.623 24.775 56.402 1.00 25.26 ATOM 453 CB TRP 263 15.831 23.406 57.052 1.00 23.10 ATOM 454 CG TRP 263 15.102 22.286 56.409 1.00 24.27 ATOM 455 CD2 TRP 263 13.881 21.697 56.873 1.00 24.86 ATOM 456 CE2 TRP 263 13.536 20.681 55.962 1.00 25.93 ATOM 457 CE3 TRP 263 13.051 21.936 57.974 1.00 24.53 ATOM 458 CD1 TRP 263 15.441 21.624 55.267 1.00 24.80

MOTA	459 NE1 TRP 263 14.501 20.655 54.990 1.00 27.16
ATOM	460 CZ2 TRP 263 12.391 19.895 56.115 1.00 26.26
ATOM	461 CZ3 TRP 263 11.911 21.151 58.132 1.00 23.32
ATOM	462 CH2 TRP 263 11.598 20.144 57.204 1.00 23.73
ATOM	463 C TRP 263 14.125 25.047 56.175 1.00 24.66
ATOM	464 O TRP 263 13.645 25.081 55.037 1.00 25.81
ATOM	465 N ALA 264 13.391 25.278 57.252 1.00 24.56
MOTA	466 CA ALA 264 11.949 25.506 57.103 1.00 25.04
ATOM	467 CB ALA 264 11.304 25.733 58.464 1.00 26.00
ATOM	468 C ALA 264 11.675 26.701 56.205 1.00 27.22
ATOM	469 O ALA 264 10.838 26.640 55.293 1.00 24.71
ATOM	470 N ARG 265 12.372 27.794 56.489 1.00 28.16
ATOM	471 CA ARG 265 12.227 29.024 55.724 1.00 32.11
ATOM	472 CB ARG 265 13.250 30.066 56.218 1.00 33.47
ATOM	473 CG ARG 265 13.155 31.408 55.520 1.00 36.25
ATOM	474 CD ARG 265 14.169 32.397 56.078 1.00 39.06
ATOM	475 NE ARG 265 15.545 31.972 55.823 1.00 42.06
ATOM	476 CZ ARG 265 16.609 32.534 56.391 1.00 43.94
ATOM	477 NH1 ARG 265 16.447 33.541 57.244 1.00 44.49
ATOM	478 NH2 ARG 265 17.827 32.092 56.110 1.00 43.52
ATOM	479 C ARG 265 12.424 28.767 54.225 1.00 32.76
ATOM	480 O ARG 265 11.843 29.460 53.392 1.00 35.61
ATOM	481 N ASP 266 13.227 27.771 53.872 1.00 33.71
ATOM	482 CA ASP 266 13.465 27.492 52.466 1.00 34.17
ATOM	483 CB ASP 266 14.931 27.106 52.236 1.00 37.32
ATOM	484 CG ASP 266 15.879 28.293 52.374 1.00 40.62
ATOM	485 OD1 ASP 266 15.556 29.392 51.866 1.00 40.66
ATOM	486 OD2 ASP 266 16.959 28.128 52.985 1.00 43.94
ATOM	487 C ASP 266 12.544 26.447 51.833 1.00 33.93
ATOM	488 O ASP 266 12.664 26.156 50.646 1.00 32.38
ATOM	489 N ILE 267 11.640 25.869 52.619 1.00 32.18
ATOM	490 CA ILE 267 10.694 24.897 52.077 1.00 30.21
ATOM	491 CB ILE 267 9.820 24.279 53.210 1.00 29.16
ATOM	492 CG2 ILE 267 8.586 23.588 52.620 1.00 31.21
ATOM	493 CG1 ILE 267 10.643 23.291 54.038 1.00 29.01
ATOM	494 CD1 ILE 267 11.069 22.051 53.278 1.00 28.89

- 40 -

	ATOM	495 C ILE 267	9.800 25.670 51.093 1.00 30.06	
	ATOM	496 O ILE 267	9.256 26.715 51.421 1.00 29.41	
	ATOM	497 N PRO 268	9.653 25.164 49.862 1.00 31.41	
	ATOM	498 CD PRO 268	10.216 23.921 49.300 1.00 31.06	
5	ATOM	499 CA PRO 268	8.813 25.857 48.879 1.00 31.62	
	ATOM	500 CB PRO 268	8.686 24.830 47.755 1.00 31.63	
	ATOM	501 CG PRO 268	10.012 24.126 47.811 1.00 34.16	
	ATOM	502 C PRO 268	7.459 26.286 49.444 1.00 31.83	
	ATOM	503 O PRO 268	6.762 25.483 50.051 1.00 31.61	
10	ATOM	504 N HIS 269	7.128 27.566 49.267 1.00 31.08	
	ATOM	505 CA HIS 269	5.867 28.164 49.715 1.00 31.47	
	ATOM	506 CB HIS 269	4.677 27.277 49.300 1.00 33.82	
	ATOM	507 CG HIS 269	4.710 26.845 47.865 1.00 36.44	
	ATOM	508 CD2 HIS 269	4.694 25.611 47.305 1.00 37.13	
15	ATOM	509 ND1 HIS 269	4.734 27.740 46.816 1.00 39.48	
	ATOM	510 CE1 HIS 269	4.731 27.078 45.672 1.00 37.91	
	ATOM	511 NE2 HIS 269	4.706 25.785 45.941 1.00 39.31	
	ATOM	512 C HIS 269	5.745 28.465 51.210 1.00 30.01	
	ATOM	513 O HIS 269	4.796 29.133 51.638 1.00 28.74	
20	MOTA	514 N PHE 270	6.693 27.994 52.012 1.00 28.26	
	MOTA	515 CA PHE 270	6.607 28.222 53.454 1.00 27.87	
			7.728 27.468 54.178 1.00 26.66	
	MOTA	517 CG PHE 270	7.661 27.563 55.684 1.00 24.18	
	MOTA	518 CD1 PHE 270	6.867 26.683 56.415 1.00 24.15	
25	MOTA	519 CD2 PHE 270	8.385 28.536 56.372 1.00 26.34	
	ATOM	520 CE1 PHE 270	6.792 26.775 57.822 1.00 22.45	
	ATOM	521 CE2 PHE 270	8.316 28.637 57.778 1.00 24.45	
	MOTA	522 CZ PHE 270	7.516 27.754 58.494 1.00 23.03	
	ATOM	523 C PHE 270	6.650 29.707 53.811 1.00 28.65	
30	MOTA	524 O PHE 270	5.866 30.175 54.634 1.00 29.19	
	ATOM	525 N SER 271	7.558 30.448 53.184 0.50 29.83	AC1
	ATOM	526 CA SER 271	7.676 31.876 53.463 0.50 31.34	AC1
	ATOM	527 CB SER 271	8.959 32.432 52.839 0.50 31.74	AC1
	ATOM	528 OG SER 271	10.104 31.869 53.460 0.50 31.64	AC1
35	ATOM	529 C SER 271	6.458 32.663 52.974 0.50 32.85	AC1
	ATOM	530 O SER 271	6.301 33.839 53.296 0.50 33.99	AC1

- 41 -

ATOM	531 N GLN 272	5.599 32.009 52.197 1.00 33.79
MOTA	532 CA GLN 272	4.378 32.642 51.696 1.00 35.22
ATOM	533 CB GLN 272	3.910 31.928 50.423 1.00 39.02
ATOM	534 CG GLN 272	4.777 32.210 49.191 1.00 43.59
ATOM	535 CD GLN 272	4.608 31.169 48.086 1.00 45.89
ATOM	536 OE1 GLN 272	3.488 30.794 47.727 1.00 47.68
ATOM	537 NE2 GLN 272	5.729 30.703 47.534 1.00 48.15
ATOM	538 C GLN 272	3.255 32.633 52.742 1.00 35.20
MOTA	539 O GLN 272	2.288 33.397 52.648 1.00 33.55
ATOM	540 N LEU 273	3.383 31.756 53.736 1.00 33.18
ATOM	541 CA LEU 273	2.402 31.651 54.811 1.00 31.26
ATOM	542 CB LEU 273	2.695 30.398 55.653 1.00 30.14
ATOM	543 CG LEU 273	2.671 29.015 54.988 1.00 29.04
ATOM	544 CD1 LEU 273	3.273 27.989 55.930 1.00 28.99
ATOM	545 CD2 LEU 273	1.231 28.638 54.645 1.00 29.21
ATOM	546 C LEU 273	2.500 32.880 55.722 1.00 30.95
ATOM	547 O LEU 273	3.556 33.513 55.793 1.00 30.58
ATOM	548 N GLU 274	1.416 33.208 56.420 1.00 31.28
ATOM	549 CA GLU 274	1.435 34.332 57.355 1.00 32.85
ATOM	550 CB GLU 274	0.154 34.378 58.195 1.00 35.60
ATOM	551 CG GLU 274	-1.039 35.022 57.511 1.00 40.50
ATOM	552 CD GLU 274	-0.954 36.543 57.494 1.00 43.35
ATOM	553 OE1 GLU 274	-1.788 37.171 56.807 1.00 44.88
ATOM	554 OE2 GLU 274	-0.062 37.109 58.169 1.00 45.29
ATOM	555 C GLU 274	2.615 34.079 58.287 1.00 32.91
ATOM	556 O GLU 274	2.867 32.936 58.693 1.00 31.56
ATOM	557 N MET 275	3.331 35.136 58.632 1.00 31.54
ATOM	558 CA MET 275	4.483 35.010 59.507 1.00 31.78
ATOM	559 CB MET 275	5.094 36.392 59.748 1.00 34.73
ATOM	560 CG MET 275	6.288 36.403 60.673 1.00 37.61
ATOM	561 SD MET 275	7.574 35.262 60.158 1.00 39.49
ATOM	562 CE MET 275	7.940 35.869 58.496 1.00 39.54
ATOM	563 C MET 275	4.149 34.351 60.838 1.00 31.91
ATOM	564 O MET 275	4.885 33.474 61.305 1.00 31.90
ATOM	565 N GLU 276	3.052 34.764 61.458 1.00 31.07
ATOM	566 CA GLU 276	2.684 34.184 62.736 1.00 30.79

ATOM 567 CB GLU 276 1.499 34.938 63.341 1.00 35.06 ATOM 568 CG GLU 276 1.866 36.382 63.755 1.00 37.66 ATOM 569 CD GLU 276 3.043 36.434 64.731 1.00 40.34 ATOM 570 OE1 GLU 276 2.978 35.751 65.774 1.00 41.45 5 571 OE2 GLU 276 4.034 37.157 64.464 1.00 42.59 ATOM ATOM 572 C GLU 276 2.388 32.693 62.596 1.00 29.05 ATOM 573 O GLU 276 2.529 31.946 63.559 1.00 28.93 ATOM 574 N ASP 277 1.973 32.250 61.411 1.00 26.93 ATOM 575 CA ASP 277 1.716 30.817 61.223 1.00 24.95 10 ATOM 576 CB ASP 277 0.817 30.565 60.005 1.00 26.30 ATOM 577 CG ASP 277 -0.656 30.768 60.320 1.00 26.04 ATOM 578 OD1 ASP 277 -0.984 31.102 61.476 1.00 29.19 ATOM 579 OD2 ASP 277 -1.492 30.596 59.410 1.00 26.42 ATOM 580 C ASP 277 3.056 30.089 61.069 1.00 25.34 15 ATOM 581 O ASP 277 3.226 28.967 61.579 1.00 25.43 ATOM 582 N GLN 278 4.007 30.721 60.373 1.00 23.47 ATOM 583 CA GLN 278 5.338 30.132 60.203 1.00 23.93 ATOM 584 CB GLN 278 6.275 31.094 59.467 1.00 23.08 ATOM 585 CG GLN 278 5.931 31.265 57.999 1.00 26.36 20 ATOM 586 CD GLN 278 6.858 32.238 57.324 1.00 26.00 ATOM 587 OE1 GLN 278 8.075 32.122 57.439 1.00 26.10 ATOM 588 NE2 GLN 278 6.293 33.210 56.609 1.00 28.94 ATOM 589 C GLN 278 5.917 29.850 61.588 1.00 22.78 ATOM 590 O GLN 278 6.445 28.765 61.857 1.00 20.87 25 ATOM 591 N ILE 279 5.821 30.849 62.461 1.00 23.32 ATOM 592 CA ILE 279 6.322 30.719 63.825 1.00 22.80 ATOM 593 CB ILE 279 6.125 32.046 64.591 1.00 24.62 ATOM 594 CG2 ILE 279 6.449 31.868 66.076 1.00 24.08 **ATOM** 595 CG1 ILE 279 6.997 33.125 63.943 1.00 27.52 30 ATOM 596 CD1 ILE 279 6.728 34.543 64.464 1.00 27.69 ATOM 597 C ILE 279 5.638 29.560 64.573 1.00 22.81 ATOM 598 O ILE 279 6.294 28.758 65.215 1.00 23.50 ATOM 599 N LEU 280 4.318 29.463 64.498 1.00 20.16 ATOM 600 CA LEU 280 3.653 28.382 65.186 1.00 18.30 35 ATOM 601 CB LEU 280 2.125 28.553 65.113 1.00 19.64 ATOM 602 CG LEU 280 1.589 29.739 65.931 1.00 22.60

10

15

20

25

30

35

ATOM 603 CD1 LEU 280 0.093 29.931 65.623 1.00 24.59 ATOM 604 CD2 LEU 280 1,759 29,496 67,399 1,00 25,05 ATOM 605 C LEU 280 4.045 27.028 64.653 1.00 17.14 ATOM 606 O LEU 280 4.160 26.084 65.436 1.00 18.84 4.225 26.905 63.335 1.00 17.52 ATOM 607 N LEU 281 MOTA 608 CA LEU 281 4.586 25.591 62.773 1.00 19.05 ATOM 609 CB LEU 281 4.550 25.618 61.241 1.00 19.60 ATOM 610 CG LEU 281 3.167 25.782 60.595 1.00 21.40 ATOM 611 CD1 LEU 281 3.324 25.870 59.073 1.00 23.62 ATOM 612 CD2 LEU 281 2.266 24.621 60.975 1.00 21.20 ATOM 613 C LEU 281 5.968 25.143 63.255 1.00 19.84 ATOM 614 O LEU 281 6.164 23.977 63.620 1.00 19.38 ATOM 615 N ILE 282 6.923 26.067 63.269 1.00 20.43 ATOM 616 CA ILE 282 8.270 25.740 63.731 1.00 19.64 ATOM 617 CB ILE 282 9,274 26,881 63,361 1,00 20,44 ATOM 618 CG2 ILE 282 10.619 26.706 64.102 1.00 20.04 ATOM 619 CG1 ILE 282 9.486 26.873 61.839 1.00 20.45 ATOM 620 CD1 ILE 282 10.278 28.076 61.323 1.00 22.03 ATOM 621 C ILE 282 8.255 25.496 65.239 1.00 19.41 ATOM 622 O ILE 282 8.894 24.574 65.717 1.00 19.21 ATOM 623 N LYS 283 7.533 26.322 65.992 1.00 17.59 ATOM 624 CA LYS 283 7.480 26.148 67.446 1.00 19.01 ATOM 625 CB LYS 283 6.624 27.246 68.103 1.00 19.89 ATOM 626 CG LYS 283 6.596 27.154 69.613 1.00 23.82 ATOM 627 CD LYS 283 5.948 28.388 70.243 1.00 26.99 ATOM 628 CE LYS 283 5.645 28.183 71.731 1.00 30.98 ATOM 629 NZ LYS 283 6.837 27.917 72.599 1.00 34.38 ATOM 630 C LYS 283 6.873 24.791 67.778 1.00 19.44 ATOM 631 O LYS 283 7.274 24.120 68.729 1.00 19.31 ATOM 632 N GLY 284 5.882 24.390 66.983 1.00 19.18 ATOM 633 CA GLY 284 5,240 23,124 67,254 1,00 18,56 ATOM 634 C GLY 284 5.981 21.885 66.806 1.00 18.31 ATOM 635 O GLY 284 5.731 20.805 67.328 1.00 19.56 ATOM 636 N SER 285 6.941 22.024 65.895 1.00 18.65 ATOM 637 CA SER 285 7.633 20.844 65.384 1.00 17.51 ATOM 638 CB SER 285 7.453 20.755 63.870 1.00 19.70

- 44 -

	ATOM	639 OG SER 285	8.063 21.874 63.212 1.00 18.48
	ATOM	640 C SER 285	9.136 20.728 65.663 1.00 15.25
	ATOM	641 O SER 285	9.705 19.673 65.406 1.00 15.43
	ATOM	642 N TRP 286	9.770 21.759 66.203 1.00 15.99
5	ATOM	643 CA TRP 286	11.221 21.642 66.395 1.00 16.28
	ATOM	644 CB TRP 286	11.812 22.920 67.007 1.00 17.10
	ATOM	645 CG TRP 286	11.458 23.226 68.414 1.00 17.32
	ATOM	646 CD2 TRP 286	12.117 22.736 69.592 1.00 18.06
	ATOM	647 CE2 TRP 286	11.440 23.291 70.709 1.00 20.12
10	ATOM	648 CE3 TRP 286	13.208 21.882 69.815 1.00 17.92
	ATOM	649 CD1 TRP 286	10.445 24.033 68.850 1.00 18.61
	ATOM	650 NE1 TRP 286	10.427 24.076 70.227 1.00 18.32
	ATOM	651 CZ2 TRP 286	11.816 23.020 72.027 1.00 17.23
	ATOM	652 CZ3 TRP 286	13.580 21.608 71.136 1.00 18.42
15	ATOM	653 CH2 TRP 286	12.889 22.172 72.219 1.00 19.75
	ATOM	654 C TRP 286	11.668 20.443 67.219 1.00 16.59
	ATOM	655 O TRP 286	12.655 19.766 66.886 1.00 17.31
	ATOM	656 N ASN 287	10.938 20.167 68.282 1.00 15.26
	ATOM	657 CA ASN 287	11.301 19.059 69.157 1.00 14.41
20	ATOM	658 CB ASN 287	10.508 19.180 70.456 1.00 17.68
	ATOM	659 CG ASN 287	10.894 18.145 71.474 1.00 19.61
	ATOM	660 OD1 ASN 287	11.757 18.374 72.348 1.00 23.92
	ATOM	661 ND2 ASN 287	10.251 16.991 71.384 1.00 18.83
	ATOM	662 C ASN 287	11.096 17.718 68.448 1.00 14.74
25	ATOM	663 O ASN 287	11.954 16.846 68.508 1.00 16.16
	ATOM	664 N GLU 288	9.966 17.555 67.752 1.00 15.22
	ATOM	665 CA GLU 288	9.745 16.319 66.986 1.00 16.77
	ATOM	666 CB GLU 288	8.367 16.358 66.288 1.00 17.55
	ATOM	667 CG GLU 288	7.213 16.044 67.224 1.00 18.68
30	ATOM	668 CD GLU 288	5.868 16.134 66.548 1.00 23.02
	ATOM	669 OE1 GLU 288	5.786 15.849 65.342 1.00 28.18
	ATOM	670 OE2 GLU 288	4.887 16.461 67.243 1.00 29.07
	ATOM	671 C GLU 288	10.838 16.122 65.921 1.00 17.49
	ATOM	672 O GLU 288	11.338 15.014 65.743 1.00 16.93
35	ATOM	673 N LEU 289	11.193 17.204 65.220 1.00 14.56
	ATOM	674 CA LEU 289	12.196 17.130 64.173 1.00 15.76

10

15

20

25

30

35

ATOM 675 CB LEU 289 12.248 18.451 63.390 1.00 14.77 676 CG LEU 289 11.006 18.639 62.483 1.00 16.67 ATOM ATOM 677 CD1 LEU 289 10.932 20.093 62.002 1.00 18.25 ATOM 678 CD2 LEU 289 11.083 17.667 61.287 1.00 15.71 ATOM 679 C LEU 289 13,555 16,784 64,752 1,00 16,05 ATOM 680 O LEU 289 14.301 16.022 64.138 1.00 16.56 ATOM 681 N LEU 290 13.884 17.312 65.929 1.00 16.37 682 CA LEU 290 15.190 16.951 66.529 1.00 16.68 ATOM ATOM 683 CB LEU 290 15.477 17.734 67.809 1.00 17.02 ATOM 684 CG LEU 290 15 786 19 219 67 684 1 00 22 29 ATOM 685 CD1 LEU 290 16.294 19.726 69.046 1.00 23.74 ATOM 686 CD2 LEU 290 16.865 19.454 66.604 1.00 25.08 ATOM 687 C LEU 290 15.229 15.471 66.868 1.00 16.18 ATOM 688 O LEU 290 16.214 14.803 66.605 1.00 17.45 MOTA 689 N LEU 291 14.142 14.958 67.465 1.00 16.16 ATOM 690 CA LEU 291 14.088 13.553 67.826 1.00 17.64 ATOM 691 CB LEU 291 12.828 13.289 68.666 1.00 17.32 ATOM 692 CG LEU 291 12.824 13.961 70.046 1.00 20.40 ATOM 693 CD1 LEU 291 11.405 13.964 70.627 1.00 22.18 ATOM 694 CD2 LEU 291 13,789 13,222 70,971 1,00 23,46 ATOM 695 C LEU 291 14.087 12.662 66.595 1.00 15.65 ATOM 696 O LEU 291 14.645 11.569 66.611 1.00 17.39 ATOM 697 N PHE 292 13.434 13.116 65.520 1.00 14.81 MOTA 698 CA PHE 292 13.360 12.330 64.311 1.00 15.62 ATOM 699 CB PHE 292 12.392 12.993 63.314 1.00 16.43 ATOM 700 CG PHE 292 12.003 12.113 62.167 1.00 16.59 ATOM 701 CD1 PHE 292 11.588 10.812 62.389 1.00 18.96 MOTA 702 CD2 PHE 292 12.002 12.607 60.875 1.00 19.01 ATOM 703 CE1 PHE 292 11.170 10.011 61.332 1.00 20.62 ATOM 704 CF2 PHF 292 11 581 11 805 59 805 1 00 18 46 ATOM 705 CZ PHE 292 11.166 10.499 60.060 1.00 18.06 MOTA 706 C PHE 292 14.761 12.191 63.713 1.00 15.70 707 O PHE 292 MOTA 15.132 11.119 63.236 1.00 15.72 ATOM 708 N ALA 293 15.526 13.278 63.760 1.00 16.34 MOTA 709 CA ALA 293 16.906 13.267 63,232 1.00 16,73 ATOM 710 CB ALA 293 17.464 14.702 63.207 1.00 17.74

10

15

20

25

30

35

ATOM 711 C ALA 293 17.802 12.368 64.090 1.00 17.09 ATOM 712 O ALA 293 18.668 11.654 63.570 1.00 17.27 ATOM 713 N ILE 294 17.623 12.423 65.407 1.00 16.09 ATOM 714 CA ILE 294 18.389 11.569 66.312 1.00 16.22 ATOM 715 CB ILE 294 18.032 11.857 67.768 1.00 15.67 ATOM 716 CG2 ILE 294 18.584 10.765 68.679 1.00 16.66 ATOM 717 CG1 ILE 294 18.615 13.218 68.160 1.00 17.00 **ATOM** 718 CD1 ILE 294 18.206 13.635 69.535 1.00 20.77 ATOM 719 C ILE 294 18.070 10.111 65.971 1.00 16.74 ATOM 720 O ILE 294 18.954 9.296 65.833 1.00 16.38 ATOM 721 N ALA 295 16.791 9.791 65.774 1.00 16.15 722 CA ALA 295 16.452 8.420 65.424 1.00 16.99 ATOM ATOM 723 CB ALA 295 14.937 8.273 65.332 1.00 16.54 ATOM 724 C ALA 295 17.083 7.993 64.088 1.00 17.97 ATOM 725 O ALA 295 17.563 6.870 63.954 1.00 18.01 MOTA 726 N TRP 296 17.071 8.881 63.102 1.00 18.59 ATOM 727 CA TRP 296 17.625 8.570 61.782 1.00 18.81 MOTA 728 CB TRP 296 17.321 9.740 60.835 1.00 20.21 **ATOM** 729 CG TRP 296 17.849 9.622 59.451 1.00 22.61 ATOM 730 CD2 TRP 296 17.398 8.716 58.433 1.00 25.62 ATOM 731 CE2 TRP 296 18.125 9.007 57.265 1.00 26.25 ATOM 732 CE3 TRP 296 16.448 7.683 58.402 1.00 25.95 ATOM 733 CD1 TRP 296 18.807 10.403 58.871 1.00 26.23 **ATOM** 734 NE1 TRP 296 18.975 10.043 57.556 1.00 26.50 **ATOM** 735 CZ2 TRP 296 17.934 8.297 56.063 1.00 27.77 ATOM 736 CZ3 TRP 296 16.257 6.977 57.206 1.00 27.65 ATOM 737 CH2 TRP 296 16.996 7.289 56.061 1.00 25.35 738 C TRP 296 ATOM 19.133 8.299 61.878 1.00 19.53 ATOM 739 O TRP 296 19.647 7.296 61.345 1.00 21.43 740 N ARG 297 ATOM 19.833 9.147 62.623 1.00 18.58 ATOM 741 CA ARG 297 21.280 8.974 62.748 1.00 18.22 ATOM 742 CB ARG 297 21,923 10,208 63,376 1,00 18,92 ATOM 743 CG ARG 297 21.886 11.465 62.525 1.00 20.63 ATOM 744 CD ARG 297 22,792 12,530 63,137 1,00 26,15 ATOM 745 NE ARG 297 22.219 13.002 64.381 1.00 29.32 ATOM 746 CZ ARG 297 21.393 14.040 64.462 1.00 28.97

10

15

20

25

30

35

ATOM 747 NH1 ARG 297 21.066 14.720 63.373 1.00 29.81 ATOM 748 NH2 ARG 297 20.872 14.372 65.628 1.00 31.03 MOTA 749 C ARG 297 21.643 7.776 63.605 1.00 18.87 ATOM 750 O ARG 297 22,738 7,225 63,473 1,00 19,01 ATOM 751 N SER 298 20.749 7.404 64.511 1.00 17.52 MOTA 752 CA SER 298 21.023 6.293 65.414 1.00 18.09 ATOM 753 CB SER 298 20.134 6.407 66.655 1.00 18.94 **ATOM** 754 OG SER 298 20.412 7.606 67.381 1.00 18.16 ATOM 755 C SER 298 20.865 4.929 64.770 1.00 20.63 ATOM 756 O SER 298 21,310 3,925 65,336 1,00 24,22 ATOM 757 N MET 299 20.270 4.868 63.582 1.00 20.01 ATOM 758 CA MET 299 20.106 3.558 62.953 1.00 22.16 ATOM 759 CB MET 299 19.367 3.682 61.610 1.00 24.42 **ATOM** 760 CG MET 299 17.940 4.159 61.735 1.00 24.29 ATOM 761 SD MET 299 17.091 4.052 60.130 1.00 31.30 ATOM 762 CE MET 299 18.221 4.950 59.082 1.00 31.06 ATOM 763 C MET 299 21.431 2.825 62.725 1.00 25.30 ATOM 764 O MET 299 21,493 1,600 62,859 1,00 26,84 ATOM 765 N GLU 300 22.485 3.565 62.414 1.00 28.43 ATOM 766 CA GLU 300 23.775 2.944 62.117 1.00 32.11 ATOM 767 CB GLU 300 24,736 3,949 61,472 1,00 34,60 ATOM 768 CG GLU 300 25.355 4.941 62.420 1.00 40.06 ATOM 769 CD GLU 300 26.689 5.477 61.910 1.00 43.56 ATOM 770 OE1 GLU 300 27.622 4.666 61.729 1.00 46.83 ATOM 771 OE2 GLU 300 26.812 6.703 61.688 1.00 45.34 ATOM 772 C GLU 300 24.467 2.304 63.300 1.00 32.94 ATOM 773 O GLU 300 25.389 1.517 63.123 1.00 32.67 ATOM 774 N PHE 301 24.033 2.649 64.507 1.00 31.51 ATOM 775 CA PHE 301 24.632 2.094 65.710 1.00 32.60 ATOM 776 CB PHE 301 24.822 3.214 66 736 1.00 32 49 ATOM 777 CG PHE 301 25.879 4.203 66.349 1.00 34.07 ATOM 778 CD1 PHE 301 27.223 3.838 66.358 1.00 33.32 ATOM 779 CD2 PHE 301 25.537 5.483 65.929 1.00 33.10 ATOM 780 CE1 PHE 301 28.207 4.737 65.949 1.00 34.17 ATOM 781 CE2 PHE 301 26.506 6.385 65.519 1.00 34.69 ATOM 782 CZ PHE 301 27.854 6.008 65.530 1.00 33.21

10

15

20

25

30

35

783 C PHE 301 ATOM 23.820 0.940 66.301 1.00 33.77 784 O PHE 301 **ATOM** 24.127 0.441 67.377 1.00 34.55 ATOM 785 N LEU 302 22,780 0.516 65,589 1.00 34.80 ATOM 786 CA LEU 302 21.966 -0.593 66.045 1.00 36.81 787 CB LEU 302 20.641 -0.645 65.287 1.00 34.98 ATOM **ATOM** 788 CG LEU 302 19.779 0.596 65.488 1.00 31.61 ATOM 789 CD1 LEU 302 18.551 0.528 64.577 1.00 31.62 790 CD2 LEU 302 ATOM 19.386 0.717 66.955 1.00 31.48 **ATOM** 791 C LEU 302 22.744 -1.869 65.775 1.00 40.52 ATOM 792 O LEU 302 23.333 -2.038 64.701 1.00 40.16 ATOM 793 N THR 303 22,733 -2,764 66,753 1,00 44,10 ATOM 794 CA THR 303 23.422 -4.037 66.634 1.00 48.80 795 CB THR 303 ATOM 23.126 -4.933 67.850 1.00 49.83 ATOM 796 OG1 THR 303 23.211 -4.151 69.050 1.00 51.18 ATOM 797 CG2 THR 303 24.132 -6.076 67.924 1.00 51.25 ATOM 798 C THR 303 22.932 -4.731 65.368 1.00 50.84 ATOM 799 O THR 303 21.739 -4.703 65.052 1.00 50.20 ATOM 800 N ALA 304 23.864 -5.341 64.644 1.00 53.24 ATOM 801 CA ALA 304 23.538 -6.040 63.410 1.00.55.88 ATOM 802 CB ALA 304 24.739 -6.867 62.946 1.00 56.05 ATOM 803 C ALA 304 22.317 -6.942 63.575 1.00 57.61 ATOM 804 O ALA 304 22.133 -7.583 64.617 1.00 58.45 ATOM 805 N ALA 305 21.481 -6.972 62.540 1.00 59.51 ATOM 806 CA ALA 305 20.282 -7.797 62.535 1.00 60.68 ATOM 807 CB ALA 305 19.548 -7.651 61 205 1 00 60 98 ATOM 808 C ALA 305 20.714 -9.245 62.744 1.00 61.71 ATOM 809 O ALA 305 19.925 -10.029 63.319 1.00 62.15 ATOM 810 OXT ALA 305 21.848 -9.572 62.316 1.00 61.88 ATOM 811 CB ALA 316 17.484 -11.402 70.435 1.00 59.02 ATOM 812 C ALA 316 15.833 -9.781 71.403 1.00 57.95 ATOM 813 O ALA 316 15.469 -9.327 70.316 1.00 58.69 ATOM 814 N ALA 316 15.341 -12.224 71.375 1.00 58.18 ATOM 815 CA ALA 316 16.413 -11.191 71.510 1.00 58.61 ATOM 816 N ALA 317 15.747 -9.096 72.539 1.00 56.79 ATOM 817 CA ALA 317 15.218 -7.739 72.587 1.00 54.70 ATOM 818 CB ALA 317 13.813 -7.745 73.174 1.00 54.73

ATOM 819 C ALA 317 16.142 -6.871 73.437 1.00 52.91 15.697 -5.935 74.111 1.00 53.06 ATOM 820 O ALA 317 ATOM 821 N SER 318 17.430 -7.207 73.404 1.00 49.42 ATOM 822 CA SER 318 18.449 -6.478 74.151 1.00 46.14 5 ATOM 823 CB SER 318 19.830 -7.056 73.835 1.00 46.72 ATOM 824 OG SER 318 20.834 -6.462 74.639 1.00 47.98 ATOM 825 C SER 318 18.378 -5.009 73.723 1.00 43.02 ATOM 826 O SER 318 18.543 -4.686 72.541 1.00 44.27 ATOM 827 N PRO 319 18.122 -4.100 74.676 0.50 41.03 AC1 10 ATOM 828 CD PRO 319 17,740 -4,342 76,079 0,50 40,29 AC1 ATOM 829 CA PRO 319 18.033 -2.672 74.351 0.50 38.31 AC1 ATOM 830 CB PRO 319 17.690 -2.032 75.694 0.50 38.96 AC1 ATOM 831 CG PRO 319 16.927 -3.116 76.402 0.50 39.34 AC1 MOTA 832 C PRO 319 19.310 -2.080 73.756 0.50 35.85 AC1 15 ATOM 833 O PRO 319 20 394 -2 240 74 319 0 50 35 73 AC1 ATOM 834 N PRO 320 19.197 -1.403 72.599 1.00 33.69 MOTA 835 CD PRO 320 18.041 -1.404 71.692 1.00 32.09 ATOM 836 CA PRO 320 20.362 -0.784 71.952 1.00 30.83 ATOM 837 CB PRO 320 19,769 -0.083 70,722 1.00 30,11 20 MOTA 838 CG PRO 320 18.279 -0.174 70.892 1.00 32.74 MOTA 839 C PRO 320 21.008 0.185 72.949 1.00 27.19 ATOM 840 O PRO 320 20.317 0.824 73.756 1.00 27.36 ATOM 841 N GLN 321 22.328 0.297 72.890 1.00 25.76 MOTA 842 CA GLN 321 23.060 1.121 73.847 1.00 25.85 25 ATOM 843 CB GLN 321 24.262 0.329 74.357 1.00 29.20 ATOM 844 CG GLN 321 23.925 -1.090 74.757 1.00 34.12 ATOM 845 CD GLN 321 23.408 -1.197 76.163 1.00 38.11 ATOM 846 OE1 GLN 321 24.127 -0.916 77.123 1.00 40.85 ATOM 847 NE2 GLN 321 22.150 -1.617 76.302 1.00 40.57 30 ATOM 848 C GLN 321 23.546 2.495 73.423 1.00 23.90 ATOM 849 O GLN 321 23,914 3,297 74,275 1,00 24 18 ATOM 850 N LEU 322 23.536 2.790 72.128 1.00 22.59 ATOM 851 CA LEU 322 24.050 4.080 71.666 1.00 21.41 ATOM 852 CB LEU 322 25.291 3.879 70.775 1.00 22.86 35 ATOM 853 CG LEU 322 26.560 3.362 71.432 1.00 25.45 ATOM 854 CD1 LEU 322 27.625 3.130 70.345 1.00 28.06

ATOM 855 CD2 LEU 322 27.036 4.384 72.497 1.00 24.21 ATOM 856 C LEU 322 23.079 4.942 70.891 1.00 22.08 ATOM 857 O LEU 322 22.435 4.478 69.961 1.00 23.11 ATOM 858 N MET 323 23.003 6.205 71.270 1.00 20.81 5 ATOM 859 CA MET 323 22,145 7,157 70,590 1,00 21,91 ATOM 860 CB MET 323 21.213 7.835 71.598 1.00 23.20 ATOM 861 CG MET 323 20.325 8.922 70.978 1.00 22.36 ATOM 862 SD MET 323 19.196 9.636 72.187 1.00 22.04 ATOM 863 CE MET 323 18.026 8.314 72.302 1.00 22.12 10 ATOM 864 C MET 323 23.054 8.187 69.914 1.00 25.54 ATOM 865 O MET 323 24.002 8.691 70.530 1.00 25.31 ATOM 866 N CYS 324 22.781 8.506 68.650 1.00 22.41 ATOM 867 CA CYS 324 23.619 9.483 67.941 1.00 24.83 868 CB CYS 324 ATOM 23.854 9.029 66.512 1.00 23.91 15 ATOM 869 SG CYS 324 24.921 10.185 65.588 1.00 27.74 ATOM 870 C CYS 324 22,995 10,873 67,950 1,00 24,34 ATOM 871 O CYS 324 22.010 11.148 67.249 1.00 24.90 ATOM 872 N LEU 325 23.560 11.758 68.749 1.00 24.49 ATOM 873 CA LEU 325 23.038 13.114 68.843 1.00 25.66 20 ATOM 874 CB LEU 325 23,421 13,746 70,183 1,00 26,79 ATOM 875 CG LEU 325 22.935 12.964 71.421 1.00 27.19 ATOM 876 CD1 LEU 325 23.256 13.744 72.704 1.00 29.28 ATOM 877 CD2 LEU 325 21.423 12.732 71.320 1.00 27.92 ATOM 878 C LEU 325 23.513 13.990 67.682 1.00 28.10 25 ATOM 879 O LEU 325 22.860 14.978 67.344 1.00 31.20 ATOM 880 N MET 326 24.650 13.618 67.094 1.00 28.83 ATOM 881 CA MET 326 25,253 14,311 65,947 1,00 30,95 ATOM 882 CB MET 326 25,726 15,721 66,350 1,00 31,86 ATOM 883 CG MET 326 26.894 15.710 67.335 1.00 31.84 30 ATOM 884 SD MET 326 27.648 17.333 67.693 1.00 34.98 ATOM 885 CE MET 326 29.085 16.800 68.706 1.00 30.77 ATOM 886 C MET 326 26,462 13,453 65,513 1,00 33,06 ATOM 887 O MET 326 26.882 12.565 66.242 1.00 32.71 ATOM 888 N PRO 327 27.013 13.682 64.307 1.00 35.54 35 ATOM 889 CD PRO 327 26.511 14.545 63.227 1.00 35.87 ATOM 890 CA PRO 327 28.180 12.896 63.857 1.00 36.24

10

15

20

25

30

35

ATOM 891 CB PRO 327 28.508 13.519 62.503 1.00 37.87 ATOM 892 CG PRO 327 27.159 13.932 62.001 1.00 35.11 ATOM 893 C PRO 327 29.353 13.035 64.836 1.00 38.75 ATOM 894 O PRO 327 29,754 14,154 65,155 1,00 38,99 ATOM 895 N GLY 328 29.890 11.908 65.314 1.00 38.52 896 CA GLY 328 31.001 11.933 66.257 1.00 38.65 MOTA ATOM 897 C GLY 328 30.606 12.217 67.700 1.00 38.39 ATOM 898 O GLY 328 31,431 12,604 68,545 1,00 39,05 ATOM 899 N MET 329 29.326 12.020 67.994 1.00 36.32 MOTA 900 CA MET 329 28.830 12.251 69.326 1.00 34.24 ATOM 901 CB MET 329 28.343 13.693 69.451 1.00 38.91 27.462 13.991 70.649 1.00 44.24 MOTA 902 CG MET 329 MOTA 903 SD MET 329 28.233 13.696 72.235 1.00 50.95 ATOM 904 CE MET 329 26.854 12.835 73.089 1.00 48.58 ATOM 905 C MET 329 27,700 11,271 69,603 1,00 30,52 ATOM 906 O MET 329 26,647 11,331 68,975 1,00 28,92 ATOM 907 N THR 330 27.960 10.324 70.490 1.00 26.42 ATOM 908 CA THR 330 26.933 9.370 70.865 1.00 23.65 ATOM 909 CB THR 330 27.338 7.895 70.542 1.00 24.12 ATOM 910 OG1 THR 330 28.672 7.654 71.005 1.00 27.18 ATOM 911 CG2 THR 330 27.269 7.622 69.034 1.00 26.34 ATOM 912 C THR 330 26.685 9.475 72.360 1.00 23.23 ATOM 913 O THR 330 27.572 9.802 73.146 1.00 23.91 ATOM 914 N LEU 331 25.450 9.211 72.748 1.00 20.37 ATOM 915 CA LEU 331 25.082 9.213 74.142 1.00 21.33 ATOM 916 CB LEU 331 23,773 9,986 74,340 1,00 24,38 ATOM 917 CG LEU 331 23.113 9.731 75.696 1.00 25.70 ATOM 918 CD1 LEU 331 23.979 10.317 76.825 1.00 30.48 ATOM 919 CD2 LEU 331 21.723 10.348 75.694 1.00 29.64 ATOM 920 C LEU 331 24.892 7.737 74.489 1.00 21.13 ATOM 921 O LEU 331 24.158 7.026 73.819 1.00 19.21 ATOM 922 N HIS 332 25.582 7.262 75.525 1.00 18.80 ATOM 923 CA HIS 332 25.472 5.864 75.901 1.00 18.64 ATOM 924 CB HIS 332 26.740 5.417 76.658 1.00 18.77 ATOM 925 CG HIS 332 26.826 3.938 76.862 1.00 21.68 ATOM 926 CD2 HIS 332 27.533 2.991 76.205 1.00 22.97

10

15

20

25

30

35

ATOM 927 ND1 HIS 332 26.092 3.273 77.824 1.00 22.38 928 CE1 HIS 332 26.340 1.978 77,745 1.00 23.74 ATOM 27.213 1.778 76.769 1.00 25.26 ATOM 929 NE2 HIS 332 ATOM 930 C HIS 332 24.262 5.721 76.820 1.00 18.95 ATOM 931 O HIS 332 23.981 6.620 77.616 1.00 19.91 ATOM 932 N ARG 333 23.594 4.581 76.715 1.00 19.39 ATOM 933 CA ARG 333 22.394 4.282 77.509 1.00 19.71 934 CB ARG 333 21.930 2.850 77.235 1.00 20.65 ATOM ATOM 935 CG ARG 333 20.582 2.512 77.896 1.00 21.54 ATOM 936 CD ARG 333 20.018 1.212 77.353 1.00 21.69 ATOM 937 NE ARG 333 18,703 0,862 77,899 1,00 20,98 ATOM 938 CZ ARG 333 18.501 0.034 78.921 1.00 22.46 ATOM 939 NH1 ARG 333 19.535 -0.547 79.531 1.00 24.12 ATOM 940 NH2 ARG 333 17.255 -0.241 79.309 1.00 20.87 ATOM 941 C ARG 333 22 643 4 463 79 018 1 00 21 14 ATOM 942 O ARG 333 21,782 4,926 79,755 1,00 18,39 ATOM 943 N ASN 334 23.832 4.107 79.484 1.00 21.27 ATOM 944 CA ASN 334 24.114 4.259 80.910 1.00 23.47 ATOM 945 CB ASN 334 25,486 3,653 81,244 1,00 24,93 ATOM 946 CG ASN 334 25.504 2.119 81.158 1.00 25.59 ATOM 947 OD1 ASN 334 24,467 1,461 81,054 1,00 26,24 ATOM 948 ND2 ASN 334 26.707 1.544 81.204 1.00 29.08 ATOM 949 C ASN 334 24.048 5.718 81.380 1.00 22.91 ATOM 950 O ASN 334 23,649 6,000 82,530 1,00 22,99 ATOM 951 N SER 335 24.441 6.657 80.524 1.00 22.89 ATOM 952 CA SER 335 24.378 8.059 80.904 1.00 22.41 ATOM 953 CB SER 335 25.178 8.915 79.930 1.00 27.35 ATOM 954 OG SER 335 26.517 8.437 79.856 1.00 31.39 ATOM 955 C SER 335 22.908 8.484 80.939 1.00 23.03 MOTA 956 O SER 335 22 496 9 260 81 809 1 00 22 21 MOTA 957 N ALA 336 22.126 7.970 79.989 1.00 21.81 ATOM 958 CA ALA 336 20.703 8.255 79.952 1.00 21.09 ATOM 959 CB ALA 336 20.060 7.595 78.718 1.00 21.81 ATOM 960 C ALA 336 20.044 7.744 81,232 1.00 21,37 ATOM 961 O ALA 336 19.209 8.425 81.830 1.00 19.40 ATOM 962 N LEU 337 20.423 6.540 81.660 1.00 19.77

10

15

20

2.5

30

35

ATOM 963 CA LEU 337 19.860 5.960 82.865 1.00 19.59 ATOM 964 CB LEU 337 20.374 4.517 83.039 1.00 19.20 ATOM 965 CG LEU 337 19.835 3.502 82.031 1.00 20.97 ATOM 966 CD1 LEU 337 20.702 2.280 82.055 1.00 23.49 ATOM 967 CD2 LEU 337 18.391 3.164 82.329 1.00 21.07 ATOM 968 C LEU 337 20.206 6.777 84.089 1.00 20.54 ATOM 969 O LEU 337 19.364 6.997 84.985 1.00 19.57 ATOM 970 N GLN 338 21.454 7.226 84.131 1.00 21.36 ATOM 971 CA GLN 338 21,920 7,994 85,264 1,00 22,39 ATOM 972 CB GLN 338 23.439 8.206 85.179 1.00 22.44 ATOM 973 CG GLN 338 23.973 8.755 86.488 1.00 27.14 ATOM 974 CD GLN 338 25.467 9.026 86.481 1.00 29.23 ATOM 975 OF1 GLN 338 25.955 9.827 87.278 1.00 30.73 ATOM 976 NE2 GLN 338 26.196 8.360 85.596 1.00 30.79 ATOM 977 C GLN 338 21.200 9.331 85.381 1.00 23.40 ATOM 978 O GLN 338 20.894 9.790 86.490 1.00 21.75 ATOM 979 N ALA 339 20.899 9.935 84,227 1.00 22.63 ATOM 980 CA ALA 339 20.215 11.217 84.191 1.00 24.41 ATOM 981 CB ALA 339 20.430 11.903 82.832 1.00 23.46 ATOM 982 C ALA 339 18.727 11.082 84.463 1.00 24.73 ATOM 983 O ALA 339 18.059 12.084 84.641 1.00 27.16 ATOM 984 N GLY 340 18.218 9.850 84.499 1.00 22.58 ATOM 985 CA GLY 340 16.803 9.622 84.754 1.00 23.89 ATOM 986 C GLY 340 15.898 9.580 83.531 1.00 25.09 14.666 9.607 83.666 1.00 25.54 ATOM 987 O GLY 340 ATOM 988 N VAL 341 16.492 9.479 82.346 1.00 23.51 ATOM 989 CA VAL 341 15.719 9.473 81.095 1.00 20.92 ATOM 990 CB VAL 341 16.134 10.677 80.211 1.00 21.83 ATOM 991 CG1 VAL 341 15.838 11.981 80.942 1.00 21.94 ATOM 992 CG2 VAL 341 17.621 10.577 79.858 1.00 21.91 ATOM 993 C VAL 341 15.891 8.185 80.300 1.00 20.24 ATOM 994 O VAL 341 15.803 8.182 79.083 1.00 19.53 ATOM 995 N GLY 342 16.132 7.079 80.999 1.00 19.65 ATOM 996 CA GLY 342 16.324 5.827 80.301 1.00 18.76 ATOM 997 C GLY 342 15.104 5.352 79.541 1.00 19.27 ATOM 998 O GLY 342 15,230 4,771 78,470 1,00 18,82

10

15

20

25

30

35

ATOM 999 N GLN 343 13.922 5.598 80.088 0.50 18.31 AC1 ATOM 1000 CA GLN 343 12.706 5.163 79.422 0.50 19.11 AC1 ATOM 1001 CB GLN 343 11.507 5.485 80.305 0.50 19.94 AC1 ATOM 1002 CG GLN 343 10.200 4.866 79.867 0.50 22.91 AC1 ATOM 1003 CD GLN 343 9 082 5 177 80 852 0.50 24 13 AC1 ATOM 1004 OE1 GLN 343 8.669 6.326 80.995 0.50 26.85 AC1 ATOM 1005 NE2 GLN 343 8.606 4.154 81.555 0.50 25.40 AC1 ATOM 1006 C GLN 343 12.542 5.813 78.043 0.50 19.14 AC1 ATOM 1007 O GLN 343 12.318 5.127 77.050 0.50 18.83 AC1 ATOM 1008 N H F 344 12.664 7.136 77.977 1.00 17.95 ATOM 1009 CA ILE 344 12.506 7.812 76.693 1.00 17.74 ATOM 1010 CB ILE 344 12.348 9.372 76.875 1.00 18.47 ATOM 1011 CG2 ILE 344 13,700 10,010 77,231 1,00 20,66 ATOM 1012 CG1 ILE 344 11.754 9.984 75.596 1.00 19.04 ATOM 1013 CD1 ILE 344 11.445 11.499 75.662 1.00 21.07 ATOM 1014 C ILE 344 13.641 7.448 75.718 1.00 17.34 ATOM 1015 O ILE 344 13.440 7.389 74.499 1.00 16.12 ATOM 1016 N PHE 345 14.844 7.210 76.248 1.00 16.60 ATOM 1017 CA PHE 345 15.976 6.826 75.417 1.00 17.63 ATOM 1018 CB PHE 345 17.208 6.636 76.322 1.00 17.86 ATOM 1019 CG PHE 345 18.455 6.189 75.613 1.00 18.24 ATOM 1020 CD1 PHE 345 18.657 4.848 75.273 1.00 18.20 ATOM 1021 CD2 PHE 345 19.470 7.090 75.363 1.00 20.10 ATOM 1022 CE1 PHE 345 19.854 4.412 74.706 1.00 19.01 ATOM 1023 CE2 PHE 345 20.663 6.673 74.798 1.00 17.96 ATOM 1024 CZ PHE 345 20.861 5.328 74.469 1.00 18.58 ATOM 1025 C PHE 345 15.603 5.522 74.710 1.00 18.98 ATOM 1026 O PHE 345 15.756 5.389 73.491 1.00 18.15 ATOM 1027 N ASP 346 15.072 4.568 75.480 1.00 18.04 ATOM 1028 CA ASP 346 14.695 3.300 74.894 1.00 18.83 14.285 2.302 75.988 1.00 19.96 ATOM 1029 CB ASP 346 ATOM 1030 CG ASP 346 15,467 1,768 76,786 1,00 24,04 ATOM 1031 OD1 ASP 346 16.630 2.038 76.430 1.00 24.95 15.232 1.043 77.784 1.00 24.86 ATOM 1032 OD2 ASP 346 ATOM 1033 C ASP 346 13.550 3.462 73.872 1.00 18.04 ATOM 1034 O ASP 346 13.549 2.782 72.841 1.00 19.39

10

15

20

25

30

35

ATOM 1035 N ARG 347 12.603 4.359 74.138 1.00 19.77 ATOM 1036 CA ARG 347 11.493 4.579 73.188 1.00 20.42 ATOM 1037 CB ARG 347 10.443 5.558 73.708 1.00 24.20 ATOM 1038 CG ARG 347 9.527 5.024 74.786 1.00 26.30 ATOM 1039 CD ARG 347 8.310 5.929 74.937 1.00 28.76 ATOM 1040 NE ARG 347 7.383 5.807 73.813 1.00 29.58 ATOM 1041 CZ ARG 347 6.312 6.577 73.629 1.00 31.91 ATOM 1042 NH1 ARG 347 6.028 7.536 74,492 1.00 32.14 ATOM 1043 NH2 ARG 347 5.522 6.378 72.579 1.00 32.47 ATOM 1044 C ARG 347 12.012 5.120 71.875 1.00 20.09 ATOM 1045 O ARG 347 11.586 4.703 70.806 1.00 18.14 ATOM 1046 N VAL 348 12.939 6.073 71.945 1.00 18.48 ATOM 1047 CA VAL 348 13.480 6.621 70.708 1.00 18.94 ATOM 1048 CB VAL 348 14.532 7.713 70.991 1.00 18.19 ATOM 1049 CG1 VAI 348 15 286 8 052 69 706 1 00 18 18 ATOM 1050 CG2 VAL 348 13.862 8.930 71.600 1.00 19.11 ATOM 1051 C VAL 348 14.143 5.518 69.882 1.00 18.63 ATOM 1052 O VAL 348 13.885 5.380 68.691 1.00 17.99 ATOM 1053 N LEU 349 14.981 4.709 70.514 1.00 18.35 ATOM 1054 CA LEU 349 15.679 3.686 69.749 1.00 19.38 ATOM 1055 CB LEU 349 16.906 3.175 70.526 1.00 20.34 ATOM 1056 CG LEU 349 17.920 4.286 70.807 1.00 20.49 ATOM 1057 CD1 LEU 349 19.173 3.626 71.408 1.00 23.32 ATOM 1058 CD2 LEU 349 18.273 5.078 69.500 1.00 18.92 ATOM 1059 C LEU 349 14.822 2.509 69.294 1.00 20.39 ATOM 1060 O LEU 349 15.112 1.901 68.263 1.00 19.62 ATOM 1061 N SER 350 13.746 2.208 70.025 1.00 21.15 ATOM 1062 CA SER 350 12.907 1.074 69.623 1.00 23.27 ATOM 1063 CB SER 350 12.443 0.294 70.855 1.00 25.65 ATOM 1064 OG SER 350 11.622 1.081 71.687 1.00 28.64 11.698 1.451 68.766 1.00 21.84 ATOM 1065 C SER 350 ATOM 1066 O SER 350 11.424 0.790 67.762 1.00 25.35 ATOM 1067 N GLU 351 10.986 2.516 69.131 1.00 22.62 ATOM 1068 CA GLU 351 9.801 2.906 68.368 1.00 22.04 ATOM 1069 CB GLU 351 8.834 3.680 69.252 1.00 22.43 ATOM 1070 CG GLU 351 8.454 2.916 70.486 1.00 26.86

10

15

20

25

30

35

ATOM 1071 CD GLU 351 7.434 3.650 71.303 1.00 28.97 ATOM 1072 OE1 GLU 351 7.473 3.544 72.548 1.00 31.85 ATOM 1073 OE2 GLU 351 6.581 4.330 70.691 1.00 32.68 ATOM 1074 C GLU 351 10.133 3.708 67.132 1.00 22.11 ATOM 1075 O GLU 351 9.348 3.766 66.183 1.00 22.30 ATOM 1076 N LEU 352 11,309 4,328 67,113 1,00 19,99 ATOM 1077 CA LEU 352 11,696 5.083 65,934 1.00 19.01 ATOM 1078 CB LEU 352 12.043 6.555 66.293 1.00 18.64 ATOM 1079 CG LEU 352 10.911 7.365 66.950 1.00 19.12 ATOM 1080 CD1 LFU 352 11 445 8 742 67 339 1 00 19 51 ATOM 1081 CD2 LEU 352 9.703 7.505 66.018 1.00 19.25 ATOM 1082 C LEU 352 12.859 4.467 65.163 1.00 19.51 ATOM 1083 O LEU 352 12.704 3.977 64.038 1.00 21.10 ATOM 1084 N SER 353 14.052 4.464 65.754 0.50 18.72 AC1 ATOM 1085 CA SER 353 15 203 3 933 65 034 0.50 18 55 AC1 ATOM 1086 CB SER 353 16.473 4.032 65.883 0.50 16.66 AC1 ATOM 1087 OG SER 353 16.782 5.378 66.160 0.50 11.47 AC1 ATOM 1088 C SER 353 15.045 2.500 64.546 0.50 19.60 AC1 ATOM 1089 O SER 353 15.207 2.236 63.355 0.50 20.26 AC1 ATOM 1090 N LEU 354 14.746 1.579 65.455 1.00 21.67 ATOM 1091 CA LEU 354 14.602 0.181 65.051 1.00 23.55 ATOM 1092 CB LEU 354 14.360 -0.715 66.278 1.00 24.35 ATOM 1093 CG LEU 354 14.284 -2.222 66.012 1.00 30.18 ATOM 1094 CD1 LEU 354 15.388 -2.664 65.055 1.00 31.88 ATOM 1095 CD2 LEU 354 14.392 -2.944 67.345 1.00 31.36 ATOM 1096 C LEU 354 13.489 -0.011 64.009 1.00 24.82 ATOM 1097 O LEU 354 13.696 -0.684 63.004 1.00 25.66 ATOM 1098 N LYS 355 12.324 0.587 64.234 1.00 26.97 ATOM 1099 CA LYS 355 11.236 0.454 63.272 1.00 26.95 ATOM 1100 CB LYS 355 10.003 1.226 63.735 1.00 29.30 ATOM 1101 CG LYS 355 9.228 0.572 64.843 1.00 34.34 ATOM 1102 CD LYS 355 8.440 -0.616 64.321 1.00 38.57 ATOM 1103 CE LYS 355 7.365 -1.007 65.319 1.00 39.54 ATOM 1104 NZ LYS 355 7.883 -0.958 66.713 1.00 40.20 ATOM 1105 C LYS 355 11.637 0.964 61.899 1.00 27.30 ATOM 1106 O LYS 355 11.281 0.369 60.883 1.00 28.58

10

15

20

25

30

35

ATOM 1107 N MET 356 12.362 2.080 61.860 1.00 25.41 ATOM 1108 CA MET 356 12.787 2.641 60.594 1.00 25.37 ATOM 1109 CB MET 356 13.279 4.071 60.778 1.00 27.04 ATOM 1110 CG MET 356 12.126 5.017 60.918 1.00 26.57 ATOM 1111 SD MET 356 12.669 6.671 60.768 1.00 36.72 ATOM 1112 CE MET 356 13.015 6.835 62.357 1.00 16.80 ATOM 1113 C MET 356 13.836 1.808 59.896 1.00 26.93 ATOM 1114 O MET 356 13.907 1.807 58.676 1.00 25.41 14.672 1.114 60.661 1.00 27.88 ATOM 1115 N ARG 357 ATOM 1116 CA ARG 357 15.656 0.281 60.003 1.00 29.75 ATOM 1117 CB ARG 357 16.733 -0.214 60.961 1.00 31.09 ATOM 1118 CG ARG 357 17.748 -1.056 60.213 1.00 35.17 ATOM 1119 CD ARG 357 18.840 -1.607 61.112 1.00 38.46 ATOM 1120 NE ARG 357 18.313 -2.543 62.097 1.00 41.53 ATOM 1121 CZ ARG 357 19.066 -3.164 63.003 1.00 43.38 ATOM 1122 NH1 ARG 357 20.376 -2.942 63.037 1.00 42.92 ATOM 1123 NH2 ARG 357 18.512 -3.995 63.879 1.00 43.48 ATOM 1124 C ARG 357 14.926 -0.925 59.422 1.00 29.63 ATOM 1125 O ARG 357 15.218 -1.353 58.310 1.00 29.83 ATOM 1126 N THR 358 13 966 -1 452 60 171 1 00 29 51 ATOM 1127 CA THR 358 13.204 -2.609 59.704 1.00 30.65 ATOM 1128 CB THR 358 12.273 -3.117 60.812 1.00 31.00 ATOM 1129 OG1 THR 358 13.071 -3.609 61.895 1.00 32.46 ATOM 1130 CG2 THR 358 11.374 -4.260 60.306 1.00 34.28 ATOM 1131 C THR 358 12.408 -2.281 58.438 1.00 30.73 ATOM 1132 O THR 358 12.286 -3.114 57.533 1.00 32.33 ATOM 1133 N LEU 359 11.895 -1.056 58.359 1.00 29.40 ATOM 1134 CA LEU 359 11.124 -0.610 57.201 1.00 29.68 ATOM 1135 CB LEU 359 10.242 0.583 57.605 1.00 30.32 ATOM 1136 CG LEU 359 8.732 0.609 57.321 1.00 34.26 ATOM 1137 CD1 LEU 359 8.197 2.038 57.529 1.00 33.77 ATOM 1138 CD2 LEU 359 8.452 0.142 55.900 1.00 34 08 ATOM 1139 C LEU 359 12.046 -0.168 56.066 1.00 28.77 ATOM 1140 O LEU 359 11.585 0.164 54.974 1.00 27.98 ATOM 1141 N ARG 360 13.349 -0.130 56.327 1.00 30.53 ATOM 1142 CA ARG 360 14.315 0.310 55.327 1.00 30.15

10

15

20

25

30

35

14.381 -0.695 54.178 1.00 33.80 ATOM 1143 CB ARG 360 14.798 -2.076 54.625 1.00 36.43 ATOM 1144 CG ARG 360 ATOM 1145 CD ARG 360 14.018 -3.165 53.900 1.00 39.56 ATOM 1146 NE ARG 360 12 588 -3.168 54.226 1.00 41.14 ATOM 1147 CZ ARG 360 11.618 -2.942 53.340 1.00 42.18 11.918 -2.688 52.071 1.00 41.02 ATOM 1148 NH1 ARG 360 ATOM 1149 NH2 ARG 360 10.345 -2.983 53,717 1.00 42.86 13.975 1.699 54.787 1.00 29.92 ATOM 1150 C ARG 360 ATOM 1151 O ARG 360 14.073 1.958 53.592 1.00 28.84 13.569 2.600 55.677 1.00 27.64 ATOM 1152 N VAL 361 ATOM 1153 CA VAL 361 13.261 3.956 55.267 1.00 25.17 ATOM 1154 CB VAL 361 12.909 4.819 56.480 1.00 24.00 ATOM 1155 CG1 VAL 361 12.684 6.254 56.066 1.00 24.37 ATOM 1156 CG2 VAL 361 11.688 4.249 57.166 1.00 23.19 ATOM 1157 C VAL 361 14.504 4.525 54.594 1.00 25.34 ATOM 1158 O VAL 361 15.613 4.407 55.133 1.00 25.79 14.344 5.109 53.404 1.00 24.62 ATOM 1159 N ASP 362 ATOM 1160 CA ASP 362 15.481 5.712 52.718 1.00 24.80 ATOM 1161 CB ASP 362 15.540 5.316 51.223 1.00 27.01 ATOM 1162 CG ASP 362 14.307 5.720 50.433 1.00 29.25 13.697 6.764 50.731 1.00 27.58 ATOM 1163 OD1 ASP 362 13.963 4.987 49.479 1.00 32.41 ATOM 1164 OD2 ASP 362 15.520 7.226 52.863 1.00 25.99 ATOM 1165 C ASP 362 ATOM 1166 O ASP 362 14.631 7.823 53.486 1.00 25.65 16.561 7.845 52.312 1.00 24.73 ATOM 1167 N GLN 363 16.742 9.286 52.405 1.00 26.50 ATOM 1168 CA GLN 363 ATOM 1169 CB GLN 363 18.044 9.682 51.690 1.00 31.84 ATOM 1170 CG GLN 363 18.339 11.179 51.662 1.00 36.89 19.008 11.689 52.921 1.00 40.13 ATOM 1171 CD GLN 363 18.615 11.346 54.047 1.00 42.87 ATOM 1172 OE1 GLN 363 20.013 12.536 52.743 1.00 40.44 ATOM 1173 NE2 GLN 363 15.540 10.070 51.855 1.00 25.17 ATOM 1174 C GLN 363 ATOM 1175 O GLN 363 15.077 11.020 52.480 1.00 22.69 15.023 9.659 50.701 1.00 24.53 ATOM 1176 N ALA 364 13.863 10.340 50.099 1.00 22.80 ATOM 1177 CA ALA 364 13.524 9.691 48.753 1.00 22.91 ATOM 1178 CB ALA 364

10

15

20

25

30

35

ATOM 1179 C ALA 364 12.631 10.326 51.022 1.00 21.81 ATOM 1180 O ALA 364 11.946 11.336 51.178 1.00 21.88 ATOM 1181 N GLU 365 12.362 9.188 51.636 1.00 22.72 ATOM 1182 CA GLU 365 11.218 9.062 52.532 1.00 21.63 ATOM 1183 CB GLU 365 10.990 7.585 52.856 1.00 22.68 ATOM 1184 CG GLU 365 10.724 6.806 51.583 1.00 23.15 ATOM 1185 CD GLU 365 10.797 5.303 51.723 1.00 28.04 11.632 4.813 52.501 1.00 26.39 ATOM 1186 OE1 GLU 365 ATOM 1187 OE2 GLU 365 10.034 4.607 51.010 1.00 27 63 ATOM 1188 C GLU 365 11.454 9.881 53.798 1.00 22.43 ATOM 1189 O GLU 365 10.557 10.570 54.298 1.00 22.18 ATOM 1190 N TYR 366 12.681 9.822 54.304 1.00 22.10 ATOM 1191 CA TYR 366 13.026 10.580 55.506 1.00 22.15 ATOM 1192 CB TYR 366 14.494 10.316 55.871 1.00 22.04 ATOM 1193 CG TYR 366 15.010 11.209 56.986 1.00 22.63 ATOM 1194 CD1 TYR 366 14.580 11.030 58.307 1.00 21.87 ATOM 1195 CE1 TYR 366 15.023 11.864 59.328 1.00 22.24 ATOM 1196 CD2 TYR 366 15.903 12.246 56.715 1.00 20.88 ATOM 1197 CE2 TYR 366 16.366 13.092 57.731 1.00 22.98 ATOM 1198 CZ TYR 366 15.913 12.899 59.041 1.00 22.25 ATOM 1199 OH TYR 366 16.315 13.752 60.054 1.00 23.04 ATOM 1200 C TYR 366 12.797 12.095 55.332 1.00 19.98 ATOM 1201 O TYR 366 12.209 12.731 56.199 1.00 19.55 ATOM 1202 N VAL 367 13,260 12,676 54,225 1,00 20,09 13.080 14.106 54.034 1.00 19.12 ATOM 1203 CA VAL 367 ATOM 1204 CB VAL 367 13.955 14.666 52.891 1.00 20.38 ATOM 1205 CG1 VAL 367 15.446 14.473 53.249 1.00 21.37 ATOM 1206 CG2 VAL 367 13.609 14.009 51.554 1.00 19.90 ATOM 1207 C VAL 367 11.607 14.458 53.784 1.00 18.65 ATOM 1208 O VAL 367 11,165 15,538 54,178 1,00 18,48 ATOM 1209 N ALA 368 10.868 13.552 53.147 1.00 20.47 ATOM 1210 CA ALA 368 9.447 13.787 52.893 1.00 19.05 ATOM 1211 CB ALA 368 8.854 12.668 51.988 1.00 18.93 ATOM 1212 C ALA 368 8.714 13.813 54.240 1.00 19.17 ATOM 1213 O ALA 368 7.863 14.682 54.487 1.00 18.81 ATOM 1214 N LEU 369 9.048 12.871 55.112 1.00 19.43

10

1.5

2.0

2.5

30

35

ATOM 1215 CA LEU 369 8.417 12.819 56.428 1.00 17.85 ATOM 1216 CB LEU 369 8.807 11.526 57.147 1.00 20.14 ATOM 1217 CG LEU 369 8.153 10.250 56.565 1.00 21.25 ATOM 1218 CD1 LEU 369 8.810 9.041 57.154 1.00 22.02 ATOM 1219 CD2 LEU 369 6.626 10.219 56.856 1.00 21.64 ATOM 1220 C LEU 369 8.772 14.076 57.235 1.00 19.07 ATOM 1221 O LEU 369 7.945 14.606 57.965 1.00 17.17 ATOM 1222 N LYS 370 10.007 14.567 57.120 1.00 18.01 ATOM 1223 CA LYS 370 10.363 15.799 57.826 1.00 19.26 ATOM 1224 CB LYS 370 11.819 16.199 57.522 1.00 18.97 ATOM 1225 CG LYS 370 12.888 15.349 58.203 1.00 21.31 ATOM 1226 CD LYS 370 14.304 15.860 57.845 1.00 25.49 ATOM 1227 CE LYS 370 14.445 17.367 58.009 1.00 25.79 ATOM 1228 NZ LYS 370 15.878 17.841 57.879 1.00 29.87 ATOM 1229 C LYS 370 9.440 16.949 57.388 1.00 17.68 ATOM 1230 O LYS 370 8.950 17.717 58.203 1.00 17.05 ATOM 1231 N ALA 371 9.209 17.075 56.081 1.00 17.98 ATOM 1232 CA ALA 371 8.368 18.154 55.596 1.00 17.26 ATOM 1233 CB ALA 371 8.344 18.154 54.065 1.00 19.00 ATOM 1234 C ALA 371 6.957 17.957 56.140 1.00 15.65 ATOM 1235 O ALA 371 6.299 18.909 56.533 1.00 17.13 ATOM 1236 N ILE 372 6.492 16.713 56.151 1.00 14.92 ATOM 1237 CA ILE 372 5.146 16.450 56.673 1.00 16.38 ATOM 1238 CB ILE 372 4.743 14.956 56.430 1.00 15.28 ATOM 1239 CG2 ILE 372 3,477 14,602 57,245 1,00 17,98 ATOM 1240 CG1 ILE 372 4.566 14.730 54.915 1.00 18.14 ATOM 1241 CD1 ILE 372 4.413 13.271 54.530 1.00 18.13 ATOM 1242 C ILE 372 5.038 16.795 58.163 1.00 16.98 ATOM 1243 O ILE 372 4.028 17.317 58.606 1.00 16.87 ATOM 1244 N ILE 373 6.089 16.522 58.942 1.00 14.47 ATOM 1245 CA ILE 373 6.080 16.829 60.369 1.00 15.13 ATOM 1246 CB ILE 373 7.392 16.251 61.042 1.00 13.81 ATOM 1247 CG2 ILE 373 7.530 16.783 62.463 1.00 15.08 ATOM 1248 CG1 ILE 373 7.340 14.717 61.052 1.00 14.66 ATOM 1249 CD1 ILE 373 8,709 14,031 61,219 1,00 17,60 ATOM 1250 C ILE 373 5.962 18.350 60.604 1.00 15.01

10

15

20

25

30

35

ATOM 1251 O ILE 373 5.212 18.817 61.477 1.00 15.67 ATOM 1252 N LEU 374 6.702 19.109 59.796 1.00 16.23 ATOM 1253 CA LEU 374 6.688 20.557 59.880 1.00 15.91 ATOM 1254 CB LEU 374 7.738 21.160 58.942 1.00 18.27 ATOM 1255 CG LEU 374 7.702 22.700 58.759 1.00 19.49 ATOM 1256 CD1 LEU 374 8.184 23.403 60.044 1.00 18.70 ATOM 1257 CD2 LEU 374 8.596 23.092 57.597 1.00 19.61 ATOM 1258 C LEU 374 5.316 21.128 59.490 1.00 17.14 ATOM 1259 O LEU 374 4.765 21.980 60.167 1.00 16.72 ATOM 1260 N LEU 375 4.803 20.662 58.367 1.00 17.78 ATOM 1261 CA LEU 375 3.561 21.202 57.831 1.00 17.01 ATOM 1262 CB LEU 375 3.573 21.071 56.301 1.00 19.06 ATOM 1263 CG LEU 375 4.788 21.715 55.581 1.00 18.84 ATOM 1264 CD1 LEU 375 4.903 21.197 54.151 1.00 18.22 ATOM 1265 CD2 LEU 375 4 644 23 234 55 610 1 00 19 41 ATOM 1266 C LEU 375 2.349 20.514 58.422 1.00 19.26 ATOM 1267 O LEU 375 1.603 19.823 57.705 1.00 19.50 ATOM 1268 N ASN 376 2.178 20.727 59.723 1.00 16.95 ATOM 1269 CA ASN 376 1.087 20.136 60.510 1.00 19.78 ATOM 1270 CB ASN 376 1.605 19.772 61.912 1.00 18.97 ATOM 1271 CG ASN 376 0.537 19.124 62.780 1.00 23.13 ATOM 1272 OD1 ASN 376 -0.527 18.732 62.289 1.00 19.72 ATOM 1273 ND2 ASN 376 0.827 18.989 64.081 1.00 21.10 ATOM 1274 C ASN 376 -0.088 21.080 60.641 1.00 17.80 ATOM 1275 O ASN 376 -0.043 22.028 61.412 1.00 18.77 ATOM 1276 N PRO 377 -1.188 20.820 59.909 1.00 20.03 ATOM 1277 CD PRO 377 -1.463 19.684 59.010 1.00 19.34 ATOM 1278 CA PRO 377 -2.342 21.728 60.011 1.00 20.40 ATOM 1279 CB PRO 377 -3.239 21.293 58.858 1.00 18.78 ATOM 1280 CG PRO 377 -2.979 19.796 58.774 1.00 19.22 ATOM 1281 C PRO 377 -3.086 21.705 61.336 1.00 21.89 ATOM 1282 O PRO 377 -3.922 22.583 61.594 1.00 22.57 ATOM 1283 N ASP 378 -2.771 20.723 62.177 1.00 20.09 ATOM 1284 CA ASP 378 -3.444 20.609 63.463 1.00 22.47 ATOM 1285 CB ASP 378 -3.608 19.131 63.809 1.00 23.71 ATOM 1286 CG ASP 378 -4.555 18.426 62.847 1.00 25.43

10

15

20

25

30

35

ATOM 1287 OD1 ASP 378 -5.579 19.028 62.487 1.00 28.35 ATOM 1288 OD2 ASP 378 -4.289 17.283 62.443 1.00 30.58 ATOM 1289 C ASP 378 -2.823 21.403 64.603 1.00 22.30 ATOM 1290 O ASP 378 -3.265 21.309 65.760 1.00 22.98 ATOM 1291 N VAL 379 -1.793 22.181 64.279 1.00 22.51 ATOM 1292 CA VAL 379 -1.167 23.053 65.266 1.00 21.52 ATOM 1293 CB VAL 379 0.044 23.807 64.662 1.00 20.60 ATOM 1294 CG1 VAL 379 0.424 25.004 65.532 1.00 22.27 ATOM 1295 CG2 VAL 379 1.226 22.848 64.516 1.00 22.31 -2.255 24.048 65.658 1.00 23.83 ATOM 1296 C VAL 379 ATOM 1297 O VAL 379 -2.918 24.655 64.793 1.00 25.06 ATOM 1298 N LYS 380 -2.460 24.212 66.958 1.00 23.33 ATOM 1299 CA LYS 380 -3.490 25.124 67.430 1.00 24.49 -3 797 24 829 68 904 1 00 25 21 ATOM 1300 CB LYS 380 ATOM 1301 CG LYS 380 -4.182 23.365 69.131 1.00 28.03 ATOM 1302 CD LYS 380 -4.460 23.035 70.594 1.00 30.82 ATOM 1303 CE LYS 380 -4.728 21.536 70.758 1.00 31.68 ATOM 1304 NZ LYS 380 -4.904 21.079 72.177 1.00 33.50 ATOM 1305 C LYS 380 -3.055 26.573 67.250 1.00 24.85 ATOM 1306 O LYS 380 -1.874 26.891 67.408 1.00 25.55 ATOM 1307 N GLY 381 -3.988 27.445 66.861 1.00 24.69 ATOM 1308 CA GLY 381 -3.647 28.852 66.704 1.00 26.29 ATOM 1309 C GLY 381 -3.384 29.378 65.295 1.00 25.30 ATOM 1310 O GLY 381 -3.246 30.598 65.093 1.00 27.29 ATOM 1311 N LEU 382 -3.313 28.490 64.311 1.00 26.35 ATOM 1312 CA LEU 382 -3.054 28.914 62.941 1.00 26.95 ATOM 1313 CB LEU 382 -2.997 27.706 61.995 1.00 25.01 ATOM 1314 CG LEU 382 -1.865 26,700 62,265 1,00 24,87 ATOM 1315 CD1 LEU 382 -2.011 25.507 61.314 1.00 24.53 ATOM 1316 CD2 LEU 382 -0.518 27.384 62.064 1.00 24.40 ATOM 1317 C LEU 382 -4.120 29.885 62.428 1.00 28.77 ATOM 1318 O LEU 382 -5.310 29.719 62.695 1.00 28.39 ATOM 1319 N LYS 383 -3.660 30.881 61.681 1.00 30.83 ATOM 1320 CA LYS 383 -4.518 31.894 61.078 1.00 32.60 ATOM 1321 CB LYS 383 -3.670 33.104 60.699 1.00 35.65 ATOM 1322 CG LYS 383 -4.352 34.121 59.788 1.00 40.31

10

15

20

25

30

35

ATOM 1323 CD LYS 383 -5.044 35.203 60.589 1.00 42.92 ATOM 1324 CE LYS 383 -5.436 36.376 59.702 1.00 43.80 ATOM 1325 NZ LYS 383 -6.040 37.476 60.505 1.00 44.52 ATOM 1326 C LYS 383 -5.159 31.313 59.819 1.00 32.46 ATOM 1327 O LYS 383 -6 374 31 411 59 620 1 00 33 42 ATOM 1328 N ASN 384 -4.332 30.700 58.977 1.00 30.19 ATOM 1329 CA ASN 384 -4.794 30.118 57.720 1.00 29.86 ATOM 1330 CB ASN 384 -4.154 30.854 56.549 1.00 32.74 ATOM 1331 CG ASN 384 -4.460 32.336 56.570 1.00 36.46 ATOM 1332 OD1 ASN 384 -5.625 32.730 56.585 1.00 39.59 ATOM 1333 ND2 ASN 384 -3.418 33.166 56.583 1.00 37.88 ATOM 1334 C ASN 384 -4.466 28.636 57.636 1.00 26.29 ATOM 1335 O ASN 384 -3.558 28.229 56.912 1.00 26.38 ATOM 1336 N ARG 385 -5.218 27.845 58.387 1.00 24.62 ATOM 1337 CA ARG 385 -5.005 26.406 58.431 1.00 24.85 ATOM 1338 CB ARG 385 -5.994 25.779 59.413 1.00 24.62 ATOM 1339 CG ARG 385 -5.910 24.275 59.561 1.00 27.77 ATOM 1340 CD ARG 385 -6.705 23.839 60.785 1.00 30.37 ATOM 1341 NE ARG 385 -5.976 24.188 62.004 1.00.31.78 ATOM 1342 CZ ARG 385 -6.329 25.148 62.849 1.00 31.80 ATOM 1343 NH1 ARG 385 -7.432 25.867 62.629 1.00 31.71 ATOM 1344 NH2 ARG 385 -5.542 25.426 63.886 1.00 28.60 ATOM 1345 C ARG 385 -5.079 25.727 57.070 1.00 24.38 ATOM 1346 O ARG 385 -4.289 24.824 56.783 1.00 24.23 ATOM 1347 N GLN 386 -6.003 26.165 56.214 1.00 24.39 ATOM 1348 CA GLN 386 -6.128 25.542 54.906 1.00 25.99 ATOM 1349 CB GLN 386 -7.320 26.124 54.128 1.00 29.68 ATOM 1350 CG GLN 386 -7.256 27.619 53.863 1.00 34.93 ATOM 1351 CD GLN 386 -7.246 28.442 55.136 1.00 37.35 ATOM 1352 OE1 GLN 386 -8.016 28.183 56.072 1.00 39.44 ATOM 1353 NE2 GLN 386 -6.373 29.443 55.183 1.00 39.95 ATOM 1354 C GLN 386 -4.867 25.646 54.067 1.00 24.30 ATOM 1355 O GLN 386 -4.561 24.727 53.318 1.00 25.10 ATOM 1356 N GLU 387 -4.140 26.752 54.182 1.00 25.50 ATOM 1357 CA GLU 387 -2.907 26.905 53.413 1.00 25.38 ATOM 1358 CB GLU 387 -2.358 28.328 53.594 1.00 29.21

10

15

20

2.5

30

35

ATOM 1359 CG GLU 387 -3.234 29.420 52.915 1.00 33.12 ATOM 1360 CD GLU 387 -2.845 30.838 53.284 1.00 37.28 ATOM 1361 OE1 GLU 387 -1.634 31.125 53.407 1.00 40.75 ATOM 1362 OE2 GLU 387 -3.750 31.691 53.436 1.00 38.95 ATOM 1363 C GLU 387 -1.877 25.841 53.852 1.00 25.54 ATOM 1364 O GLU 387 -1.097 25.329 53.030 1.00 24.67 ATOM 1365 N VAL 388 -1.897 25.476 55.132 1.00 24.28 -0.960 24.447 55.617 1.00 21.40 ATOM 1366 CA VAL 388 ATOM 1367 CB VAL 388 -0.845 24.439 57.168 1.00 19.68 ATOM 1368 CG1 VAL 388 0.182 23.410 57.597 1.00 22.22 ATOM 1369 CG2 VAL 388 -0.477 25.824 57.691 1.00 20.28 ATOM 1370 C VAL 388 -1.444 23.076 55.178 1.00 22.10 -0.666 22.211 54.782 1.00 21.10 ATOM 1371 O VAL 388 ATOM 1372 N GLU 389 -2.750 22.859 55.243 1.00 22.00 ATOM 1373 CA GLU 389 -3.284 21.577 54.825 1.00 21.41 ATOM 1374 CB GLU 389 -4.801 21.538 54.987 1.00 22.76 ATOM 1375 CG GLU 389 -5,358 20.146 54.988 1.00 31.47 ATOM 1376 CD GLU 389 -6.793 20.093 55.471 1.00 36.14 ATOM 1377 OE1 GLU 389 -7.160 20.927 56.334 1.00 39.74 ATOM 1378 OF2 GLU 389 -7.540 19.204 55.006 1.00 39.63 ATOM 1379 C GLU 389 -2.936 21,294 53,382 1.00 19.32 ATOM 1380 O GLU 389 -2.653 20.155 53.025 1.00 21.32 ATOM 1381 N VAL 390 -3.001 22.313 52.534 1.00 19.72 ATOM 1382 CA VAL 390 -2.685 22.148 51.125 1.00 19.82 -2.950 23.447 50.316 1.00 19.77 ATOM 1383 CB VAL 390 ATOM 1384 CG1 VAL 390 -2,307 23,344 48,919 1,00 22,22 ATOM 1385 CG2 VAL 390 -4.442 23.652 50.169 1.00 23.95 -1.231 21.744 50.924 1.00 20.27 ATOM 1386 C VAL 390 ATOM 1387 O VAL 390 -0.924 20.894 50.093 1.00 20.79 ATOM 1388 N LEU 391 -0.334 22.345 51.699 1.00.21.06 ATOM 1389 CA LEU 391 1.078 22.004 51.552 1.00 19.84 ATOM 1390 CB LEU 391 1.951 22.982 52.328 1.00 20.90 ATOM 1391 CG LEU 391 1.895 24.438 51.836 1.00 21.65 2.846 25.283 52.673 1.00 23.70 ATOM 1392 CD1 LEU 391 ATOM 1393 CD2 LEU 391 2 260 24 515 50 351 1 00 25 56 ATOM 1394 C LEU 391 1.327 20.583 52.031 1.00 19.59

ATOM	1395 O LEU 391	2.090 19.837 51.421 1.00 19.63	
MOTA	1396 N ARG 392	0.680 20.192 53.130 0.50 19.30	AC1
ATOM	1397 CA ARG 392	0.862 18.823 53.628 0.50 19.65	AC1
ATOM	1398 CB ARG 392	0.212 18.620 55.016 0.50 19.22	AC1
ATOM	1399 CG ARG 392	0.060 17.123 55.382 0.50 18.74	AC1
ATOM	1400 CD ARG 392	-0.380 16.857 56.840 0.50 19.04	AC1
ATOM	1401 NE ARG 392	0.710 17.001 57.811 0.50 18.30	AC1
ATOM	1402 CZ ARG 392	0.739 16.427 59.020 0.50 18.32	AC1
ATOM	1403 NH1 ARG 392	-0.262 15.660 59.432 0.50 18.09	AC1
ATOM	1404 NH2 ARG 392	1.783 16.606 59.826 0.50 13.08	AC1
ATOM	1405 C ARG 392	0.259 17.833 52.624 0.50 19.79	AC1
ATOM	1406 O ARG 392	0.768 16.730 52.453 0.50 19.90	AC1
ATOM	1407 N GLU 393	-0.839 18.220 51.976 1.00 19.51	
ATOM	1408 CA GLU 393	-1.484 17.355 50.979 1.00 21.32	
ATOM	1409 CB GLU 393	-2.858 17.922 50.575 1.00 23.83	
ATOM	1410 CG GLU 393	-3.631 17.066 49.588 1.00 29.44	
ATOM	1411 CD GLU 393	-4.209 15.767 50.173 1.00 34.23	
ATOM	1412 OE1 GLU 393	-3.940 15.434 51.348 1.00 34.71	
ATOM	1413 OE2 GLU 393	-4.952 15.071 49.433 1.00 37.12	
ATOM	1414 C GLU 393	-0.556 17.210 49.763 1.00 21.12	
MOTA	1415 O GLU 393	-0.486 16.147 49.157 1.00 20.35	
ATOM	1416 N LYS 394	0.143 18.287 49.395 1.00 19.98	
ATOM	1417 CA LYS 394	1.102 18.186 48.302 1.00 21.24	
ATOM	1418 CB LYS 394	1.787 19.519 48.048 1.00 22.05	
ATOM	1419 CG LYS 394	0.903 20.468 47.258 1.00 24.02	
ATOM	1420 CD LYS 394	1.608 21.778 46.964 1.00 25.62	
ATOM	1421 CE LYS 394	0.690 22.711 46.199 1.00 28.47	
ATOM	1422 NZ LYS 394	1.369 24.012 45.959 1.00 30.41	
ATOM	1423 C LYS 394	2.153 17.137 48.667 1.00 22.08	
MOTA	1424 O LYS 394	2.555 16.341 47.825 1.00 20.82	
ATOM	1425 N MET 395	2.590 17.136 49.932 1.00 21.43	
ATOM	1426 CA MET 395	3.607 16.166 50.369 1.00 21.13	
ATOM	1427 CB MET 395	4.177 16.520 51.746 1.00 24.05	
ATOM	1428 CG MET 395	5.100 17.680 51.738 1.00 24.66	
ATOM	1429 SD MET 395	6.457 17.503 50.571 1.00 27.36	
ATOM	1430 CE MET 395	6.985 15.797 50.738 1.00 23.91	

4
0
-
Ď
U
U
T
8
O
Sept.
n.

10

15

20

25

30

35

3.121 14.744 50.417 1.00 20.46 ATOM 1431 C MET 395 3.872 13.832 50.095 1.00 22.42 ATOM 1432 O MET 395 ATOM 1433 N PHE 396 1.862 14.542 50.827 1.00 20.87 1 285 13.202 50.858 1.00 21.65 ATOM 1434 CA PHE 396 ATOM 1435 CB PHE 396 -0.176 13.203 51.374 1.00 20.90 -0.320 13.286 52.875 1.00 22.60 ATOM 1436 CG PHE 396 ATOM 1437 CD1 PHE 396 0.733 12.996 53.727 1.00 22.79 -1.544 13.640 53.436 1.00 23.58 ATOM 1438 CD2 PHE 396 ATOM 1439 CE1 PHE 396 0.570 13.063 55.116 1.00 20.29 ATOM 1440 CE2 PHE 396 -1.712 13.702 54.826 1.00 23.72 ATOM 1441 CZ PHE 396 -0.655 13.416 55.669 1.00 22.24 ATOM 1442 C PHE 396 1.281 12.652 49.429 1.00 22.43 1.635 11.494 49.215 1.00 21.80 ATOM 1443 O PHE 396 0.844 13.462 48.458 1.00 22.96 ATOM 1444 N LEU 397 ATOM 1445 CA LEU 397 0.813 13.022 47.061 1.00 21.97 ATOM 1446 CB LEU 397 0.139 14.099 46.176 1.00 22.88 ATOM 1447 CG LEU 397 -1.385 14.161 46.354 1.00 23.93 ATOM 1448 CD1 LEU 397 -1.981 15.078 45.315 1.00 25.27 ATOM 1449 CD2 LEU 397 -1.972 12.759 46.190 1.00 25.99 ATOM 1450 C LEU 397 2.233 12.705 46.560 1.00 24.94 2.450 11.692 45.873 1.00 25.61 ATOM 1451 O LEU 397 ATOM 1452 N CYS 398 3.195 13.548 46.924 1.00 23.80 ATOM 1453 CA CYS 398 4.593 13.333 46.519 1.00 26.51 ATOM 1454 CB CYS 398 5.509 14.454 47.041 1.00 28.87 5.551 15.910 46.032 1.00 39.48 ATOM 1455 SG CYS 398 ATOM 1456 C CYS 398 5.111 12.027 47.090 1.00 25.35 ATOM 1457 O CYS 398 5,738 11,221 46,399 1.00 25,03 ATOM 1458 N LEU 399 4.861 11.821 48.371 1.00 24.81 ATOM 1459 CA LEU 399 5.366 10.620 49.009 1.00 24.04 ATOM 1460 CB LEU 399 5 232 10 739 50 530 1.00 24.26 ATOM 1461 CG LEU 399 5.806 9.580 51.344 1.00 24.01 ATOM 1462 CD1 LEU 399 7.281 9.343 50.985 1.00 22.08 ATOM 1463 CD2 LEU 399 5.672 9.931 52.821 1.00 22.85 4.715 9.352 48.518 1.00 26.35 ATOM 1464 C LEU 399 ATOM 1465 O LEU 399 5.398 8.363 48.267 1.00 25.02 ATOM 1466 N ASP 400 3.391 9.377 48.361 1.00 27.30

Ö
100
Ü
0
4
10
U
g:
=
(Car
1
TU

10

15

20

25

30

35

ATOM 1467 CA ASP 400 2.680 8.200 47.874 1.00 29.09 ATOM 1468 CB ASP 400 1.179 8.490 47.772 1.00 31.25 ATOM 1469 CG ASP 400 0.379 7.258 47.400 1.00 34.75 ATOM 1470 OD1 ASP 400 0.236 6.356 48.252 1.00 35.16 ATOM 1471 OD2 ASP 400 -0.091 7.188 46.250 1.00 38.49 ATOM 1472 C ASP 400 3.217 7.816 46.497 1.00 28.91 ATOM 1473 O ASP 400 3,436 6,642 46,212 1,00 29,66 ATOM 1474 N GLU 401 3.420 8.813 45.644 1.00 28.16 ATOM 1475 CA GLU 401 3.936 8.577 44.299 1.00 29.87 4.052 9.895 43.533 1.00 32.50 ATOM 1476 CB GLU 401 ATOM 1477 CG GLU 401 4.735 9.751 42.180 1.00 38.83 ATOM 1478 CD GLU 401 4.784 11.048 41.406 1.00 42.93 5.449 12.003 41.865 1.00 45.46 ATOM 1479 OE1 GLU 401 ATOM 1480 OF2 GLU 401 4.147 11.114 40.334 1.00 45.87 5.308 7.911 44.360 1.00 31.19 ATOM 1481 C GLU 401 ATOM 1482 O GLU 401 5.574 6.926 43.650 1.00 31.37 ATOM 1483 N TYR 402 6.171 8.444 45.224 1.00 28.55 ATOM 1484 CA TYR 402 7.516 7.918 45.365 1.00 29.01 ATOM 1485 CB TYR 402 8.314 8.737 46.384 1.00 27.40 ATOM 1486 CG TYR 402 9.667 8.134 46.659 1.00 27.45 ATOM 1487 CD1 TYR 402 9.849 7.238 47.709 1.00 27.18 ATOM 1488 CE1 TYR 402 11.087 6.635 47.933 1.00 28.15 ATOM 1489 CD2 TYR 402 10.747 8.419 45.834 1.00 27.22 ATOM 1490 CE2 TYR 402 11.996 7.820 46.050 1.00 30.03 ATOM 1491 CZ TYR 402 12.147 6.936 47.097 1.00 30.78 ATOM 1492 OH TYR 402 13.374 6.358 47.316 1.00 31.66 ATOM 1493 C TYR 402 7.503 6.453 45.769 1.00 30.16 8.206 5.641 45.187 1.00 29.67 ATOM 1494 O TYR 402 ATOM 1495 N CYS 403 6.700 6.113 46.763 1.00 30.42 ATOM 1496 CA CYS 403 6.616 4.739 47.215 1.00 34.32 ATOM 1497 CB CYS 403 5.691 4.650 48.430 1.00 33.37 ATOM 1498 SG CYS 403 6.357 5.485 49.920 1.00 31.63 ATOM 1499 C CYS 403 6.116 3.820 46.104 1.00 36.81 ATOM 1500 O CYS 403 6.612 2.703 45.936 1.00 36.95 ATOM 1501 N ARG 404 5.140 4.289 45.335 1.00 39.50 ATOM 1502 CA ARG 404 4.597 3.453 44.271 1.00 42.67

340
4Ö
J.
100
4
1 88
U
m
20
0
1
T.
Count.
0

10

15

20

25

30

35

3,280 4.045 43.746 1.00 43.44 ATOM 1503 CB ARG 404 ATOM 1504 CG ARG 404 2.135 3.802 44.718 1.00 46.08 ATOM 1505 CD ARG 404 0.746 4.164 44.188 1.00 46.89 ATOM 1506 NE ARG 404 0.490 5.602 44.159 1.00 46.69 ATOM 1507 CZ ARG 404 0.733 6.386 43.116 1.00 47.48 1.241 5.874 42.002 1.00 48.94 ATOM 1508 NH1 ARG 404 ATOM 1509 NH2 ARG 404 0.462 7.684 43.181 1.00 48.22 5.578 3.206 43.137 1.00 43.67 ATOM 1510 C ARG 404 ATOM 1511 O ARG 404 5.640 2.102 42.598 1.00 44.97 ATOM 1512 N ARG 405 6.356 4.220 42.785 1.00 45.45 ATOM 1513 CA ARG 405 7.330 4.098 41.710 1.00 47.72 ATOM 1514 CB ARG 405 7.700 5.481 41.167 1.00 49.80 6.535 6.298 40.624 1.00 53.09 ATOM 1515 CG ARG 405 ATOM 1516 CD ARG 405 7.005 7.695 40.233 1.00 56.62 ATOM 1517 NE ARG 405 5.931 8.506 39.661 1.00 59.35 5.356 8.263 38.488 1.00 60.20 ATOM 1518 CZ ARG 405 5.753 7.231 37.756 1.00 61.80 ATOM 1519 NH1 ARG 405 ATOM 1520 NH2 ARG 405 4.382 9.049 38.046 1.00 60.75 ATOM 1521 C ARG 405 8.609 3.410 42.166 1.00 48.23 ATOM 1522 O ARG 405 9.078 2.464 41.528 1.00 48.90 9.163 3.891 43.278 1.00 47.66 ATOM 1523 N SER 406 ATOM 1524 CA SER 406 10.421 3.382 43.819 1.00 48.66 ATOM 1525 CB SER 406 11.099 4.477 44.638 1.00 49.49 ATOM 1526 OG SER 406 11.118 5.698 43.919 1.00 51.64 ATOM 1527 C SER 406 10.336 2.112 44.656 1.00 48.77 ATOM 1528 O SER 406 11.355 1.507 44.968 1.00 48.91 ATOM 1529 N ARG 407 9.129 1.711 45.026 1.00 49.27 ATOM 1530 CA ARG 407 8.948 0.500 45.813 1.00 50.47 ATOM 1531 CB ARG 407 9.106 0.811 47.302 1.00 52.25 10.476 0.434 47.849 1.00 54.88 ATOM 1532 CG ARG 407 ATOM 1533 CD ARG 407 10.942 1.401 48.918 1.00 55.39 ATOM 1534 NE ARG 407 12.157 0.927 49.573 1.00 56.11 ATOM 1535 CZ ARG 407 12.885 1.653 50.416 1.00 56.40 ATOM 1536 NH1 ARG 407 12.524 2.895 50.707 1.00 56.21 13.973 1.133 50.972 1.00 55.90 ATOM 1537 NH2 ARG 407 ATOM 1538 C ARG 407 7.586 -0.110 45.535 1.00 50.00

10

15

20

2.5

30

35

ATOM 1539 O ARG 407 6.847 -0.468 46.451 1.00 50.06 7.279 -0.233 44.248 1.00 49.76 ATOM 1540 N SER 408 ATOM 1541 CA SER 408 6.010 -0.777 43.782 1.00 49.98 ATOM 1542 CB SER 408 6.060 -0.957 42.262 1.00 50.23 ATOM 1543 OG SER 408 7 129 -1.806 41.880 1.00 50.48 ATOM 1544 C SER 408 5.622 -2.100 44.439 1.00 49.86 ATOM 1545 O SER 408 4.444 -2.354 44.698 1.00 50.10 6.620 -2.933 44.706 1.00 50.01 ATOM 1546 N SER 409 ATOM 1547 CA SER 409 6.412 -4.245 45.307 1.00 49.71 ATOM 1548 CB SER 409 7.704 -5.055 45.217 1.00 50.85 8.799 -4.306 45.730 1.00 52.55 ATOM 1549 OG SER 409 5.954 -4.195 46.758 1.00 49.15 ATOM 1550 C SER 409 ATOM 1551 O SER 409 5.476 -5.195 47.300 1.00 48.48 ATOM 1552 N GLU 410 6 095 -3 035 47 392 1 00 47 66 ATOM 1553 CA GLU 410 5.701 -2.912 48.785 1.00 45.50 ATOM 1554 CB GLU 410 6.787 -2.197 49.577 1.00 46.29 ATOM 1555 CG GLU 410 8.079 -2.980 49.712 1.00 47.76 ATOM 1556 CD GLU 410 9.074 -2.261 50.592 1.00 48.13 10.155 -1.882 50.092 1.00 49.66 ATOM 1557 OE1 GLU 410 ATOM 1558 OE2 GLU 410 8.761 -2.063 51.784 1.00 48.57 4.373 -2.197 48.973 1.00 44.10 ATOM 1559 C GLU 410 ATOM 1560 O GLU 410 4.311 -0.974 49.114 1.00 41.70 ATOM 1561 N GLU 411 3.306 -2.985 48.986 1.00 42.76 ATOM 1562 CA GLU 411 1.973 -2.451 49.154 1.00 41.57 ATOM 1563 CB GLU 411 0.945 -3.529 48.814 1.00 44.42 ATOM 1564 CG GLU 411 1.166 -4.132 47.439 1.00 48.49 ATOM 1565 CD GLU 411 0.151 -5.191 47.100 1.00 49.60 ATOM 1566 OE1 GLU 411 0.111 -6.226 47.806 1.00 49.80 ATOM 1567 OE2 GLU 411 -0.605 -4.979 46.129 1.00 50.58 ATOM 1568 C GLU 411 1.805 -2.000 50.594 1.00 38.78 ATOM 1569 O GLU 411 2.254 -2.682 51.526 1.00 38.53 ATOM 1570 N GLY 412 1.170 -0.845 50.768 1.00 34.78 ATOM 1571 CA GLY 412 0.953 -0.313 52.103 1.00 32.19 ATOM 1572 C GLY 412 2.163 0.402 52.695 1.00 29.28 2.133 0.770 53.865 1.00 28.68 ATOM 1573 O GLY 412 ATOM 1574 N ARG 413 3.207 0.625 51.901 1.00 28.70

10

15

20

25

30

35

4.413 1.286 52.407 1.00 27.65 ATOM 1575 CA ARG 413 ATOM 1576 CB ARG 413 5.513 1.319 51.348 1.00 29.50 6.850 1.839 51.905 1.00 29.56 ATOM 1577 CG ARG 413 ATOM 1578 CD ARG 413 8.004 1.721 50.903 1.00 32.68 9.242 2.244 51.484 1.00 34.48 ATOM 1579 NE ARG 413 ATOM 1580 CZ ARG 413 9.951 1.632 52.433 1.00 35.49 ATOM 1581 NH1 ARG 413 9,569 0,454 52,914 1,00 34,87 11.036 2.221 52.929 1.00 35.73 ATOM 1582 NH2 ARG 413 ATOM 1583 C ARG 413 4 153 2 715 52 874 1 00 27 61 ATOM 1584 O ARG 413 4.656 3.142 53.911 1.00 26.64 ATOM 1585 N PHE 414 3.377 3.447 52.091 1.00 27.23 3.025 4.829 52.406 1.00 25.72 ATOM 1586 CA PHE 414 ATOM 1587 CB PHE 414 2.109 5.368 51.290 1.00 27.69 ATOM 1588 CG PHE 414 1.553 6.756 51.552 1.00 26.95 2.359 7.882 51.454 1.00 28.43 ATOM 1589 CD1 PHE 414 ATOM 1590 CD2 PHE 414 0.217 6.921 51.891 1.00 29.19 ATOM 1591 CE1 PHE 414 1.842 9.165 51.692 1.00 28.49 ATOM 1592 CE2 PHE 414 -0.315 8.199 52.134 1.00 29.46 0.503 9.325 52.033 1.00 28.75 ATOM 1593 CZ PHE 414 ATOM 1594 C PHE 414 2.336 4.891 53.777 1.00 26.40 ATOM 1595 O PHE 414 2.691 5.702 54.637 1.00 26.65 ATOM 1596 N ALA 415 1.355 4.027 53.997 1.00 25.07 ATOM 1597 CA ALA 415 0.652 4.002 55.271 1.00 24.63 ATOM 1598 CB ALA 415 -0.531 3.028 55.193 1.00 23.72 ATOM 1599 C ALA 415 1 572 3 622 56 436 1 00 24 02 ATOM 1600 O ALA 415 1.433 4.142 57.547 1.00 23.15 ATOM 1601 N ALA 416 2.518 2.722 56.174 1.00 24.35 ATOM 1602 CA ALA 416 3.448 2.270 57.205 1.00 24.54 ATOM 1603 CB ALA 416 4.313 1.143 56.666 1.00 24.42 ATOM 1604 C ALA 416 4.319 3.436 57.639 1.00 23.97 ATOM 1605 O ALA 416 4.544 3.646 58.832 1.00 25.89 ATOM 1606 N LEU 417 4.799 4.192 56.664 1.00 23.99 ATOM 1607 CA LEU 417 5.638 5.348 56.952 1.00 23.65 ATOM 1608 CB LEU 417 6.056 6.013 55.651 1.00 23.88 ATOM 1609 CG LEU 417 6.940 5.132 54.768 1.00 22.81 ATOM 1610 CD1 LEU 417 7.104 5.745 53.381 1.00 25.97

10

15

20

25

30

35

8.313 4.978 55.464 1.00 24.86 ATOM 1611 CD2 LEU 417 ATOM 1612 C LEU 417 4.894 6.346 57.843 1.00 23.64 5.434 6.825 58.851 1.00 24.26 ATOM 1613 O LEU 417 ATOM 1614 N LEU 418 3.635 6.632 57.517 1.00 22.96 2.896 7.617 58.305 1.00 22.78 ATOM 1615 CA LEU 418 ATOM 1616 CB LEU 418 1.555 7.961 57.622 1.00 22.19 ATOM 1617 CG LEU 418 1.632 8.536 56.193 1.00 22.93 0.232 8.983 55.715 1.00 23.88 ATOM 1618 CD1 LEU 418 ATOM 1619 CD2 LEU 418 2 554 9 749 56 179 1.00 23.65 2.646 7.201 59.762 1.00 24.12 ATOM 1620 C LEU 418 ATOM 1621 O LEU 418 2.372 8.046 60.620 1.00 22.61 2.706 5.901 60.049 1.00 25.06 ATOM 1622 N LEU 419 ATOM 1623 CA LEU 419 2,496 5,440 61,404 1,00 27,92 ATOM 1624 CB LEU 419 2.406 3.909 61.451 1.00 31.65 ATOM 1625 CG LEU 419 1.114 3.343 60.884 1.00 34.11 ATOM 1626 CD1 LEU 419 1.026 1.848 61.218 1.00 36.06 ATOM 1627 CD2 LEU 419 -0.068 4.081 61.480 1.00 34.83 ATOM 1628 C LEU 419 3.594 5.891 62.360 1.00 29.85 3.400 5.885 63.574 1.00 31.55 ATOM 1629 O LEU 419 ATOM 1630 N ARG 420 4 736 6 296 61 828 1.00 31.33 ATOM 1631 CA ARG 420 5.801 6.725 62.718 1.00 31.87 ATOM 1632 CB ARG 420 7.145 6.755 61.985 1.00 32.74 ATOM 1633 CG ARG 420 7.648 5.387 61.490 1.00 33.67 ATOM 1634 CD ARG 420 7.856 4.364 62.622 1.00 36.93 ATOM 1635 NE ARG 420 6.709 3.481 62.820 1.00 35.35 ATOM 1636 CZ ARG 420 6.179 3.194 64.003 1.00 37.82 ATOM 1637 NH1 ARG 420 6.692 3.714 65.116 1.00 39.26 5.112 2.408 64.079 1.00 39.04 ATOM 1638 NH2 ARG 420 ATOM 1639 C ARG 420 5,477 8.092 63,303 1.00 32,15 ATOM 1640 O ARG 420 5.995 8.456 64.362 1.00 31.60 ATOM 1641 N LEU 421 4.591 8.845 62.655 1.00 30.38 ATOM 1642 CA LEU 421 4.278 10.175 63.164 1.00 29.53 ATOM 1643 CB LEU 421 3.519 10.976 62.121 1.00 30.72 ATOM 1644 CG LEU 421 4.322 11.027 60.808 1.00 31.31 ATOM 1645 CD1 LEU 421 3.645 12.019 59.885 1.00 32.38 ATOM 1646 CD2 LEU 421 5.800 11.411 61.053 1.00 31.74

10

15

20

25

30

35

ATOM 1647 C LEU 421 3.582 10.256 64.521 1.00 28.39 ATOM 1648 O LEU 421 3.977 11.061 65.363 1.00 26.36 2.533 9.446 64.762 1.00 27.69 ATOM 1649 N PRO 422 ATOM 1650 CD PRO 422 1.678 8.672 63.839 1.00 27.47 ATOM 1651 CA PRO 422 1.915 9.559 66.090 1.00 26.04 0.717 8.603 66.005 1.00 28.29 ATOM 1652 CB PRO 422 ATOM 1653 CG PRO 422 0.350 8.664 64.557 1.00 28.91 ATOM 1654 C PRO 422 2.906 9.143 67.198 1.00 25.36 ATOM 1655 O PRO 422 2.832 9.637 68.322 1.00 24.06 ATOM 1656 N ALA 423 3.821 8.228 66.872 1.00 24.34 ATOM 1657 CA ALA 423 4.817 7.779 67.840 1.00 22.88 5,589 6,599 67,273 1,00 26,29 ATOM 1658 CB ALA 423 ATOM 1659 C ALA 423 5.765 8.942 68.158 1.00 24.20 6.094 9.197 69.315 1.00 22.14 ATOM 1660 O ALA 423 6.212 9.640 67.119 1.00 22.92 ATOM 1661 N LEU 424 ATOM 1662 CA LEU 424 7.103 10.773 67.309 1.00 22.78 7.512 11.306 65.936 1.00 23.40 ATOM 1663 CB LEU 424 ATOM 1664 CG LEU 424 8.405 12.531 65.875 1.00 24.54 9.777 12.226 66.517 1.00 22.52 ATOM 1665 CD1 LEU 424 ATOM 1666 CD2 LEU 424 8.589 12.892 64.405 1.00 22.78 ATOM 1667 C LEU 424 6.422 11.861 68.153 1.00 22.46 ATOM 1668 O LEU 424 7.036 12.468 69.038 1.00 21.68 ATOM 1669 N ARG 425 5.136 12.101 67.900 1.00 22.38 ATOM 1670 CA ARG 425 4.386 13.095 68.663 1.00 23.67 ATOM 1671 CB ARG 425 2.969 13.240 68.087 1.00 26.56 ATOM 1672 CG ARG 425 2.066 14.140 68.903 1.00 30.90 ATOM 1673 CD ARG 425 0.977 14.732 68.031 1.00 36.25 0.469 13.774 67.044 1.00 40.86 ATOM 1674 NE ARG 425 ATOM 1675 CZ ARG 425 -0.070 12.592 67.339 1.00 42.76 ATOM 1676 NH1 ARG 425 -0.183 12.196 68.604 1.00 46.63 ATOM 1677 NH2 ARG 425 -0.498 11.800 66.367 1.00 44.97 ATOM 1678 C ARG 425 4.309 12.737 70.150 1.00 21.12 ATOM 1679 O ARG 425 4.418 13.604 71.021 1.00 21.30 4.124 11.452 70.436 1.00 19.60 ATOM 1680 N SER 426 ATOM 1681 CA SER 426 4.021 10.989 71.820 1.00 19.49 ATOM 1682 CB SER 426 3.534 9.539 71.855 1.00 20.63

АТОМ	1683 OG SER 426	3.491 9.086 73.198 1.00 23.17	
ATOM	1684 C SER 426	5.374 11.096 72.535 1.00 17.38	
ATOM	1685 O SER 426	5.458 11.496 73.698 1.00 18.97	
ATOM	1686 N ILE 427	6.419 10.742 71.812 1.00 18.11	
ATOM	1687 CA ILE 427	7.770 10.812 72.368 1.00 15.88	
ATOM	1688 CB ILE 427	8.763 10.095 71.449 1.00 15.75	
ATOM	1689 CG2 ILE 427	10.213 10.351 71.913 1.00 17.78	
ATOM	1690 CG1 ILE 427	8.479 8.591 71.526 1.00 18.23	
ATOM	1691 CD1 ILE 427	9.082 7.789 70.440 1.00 20.33	
ATOM	1692 C ILE 427	8.146 12.272 72.599 1.00 16.69	
ATOM	1693 O ILE 427	8.779 12.589 73.606 1.00 16.41	
ATOM	1694 N SER 428	7.767 13.159 71.685 1.00 17.02	
ATOM	1695 CA SER 428	8.059 14.590 71.884 1.00 17.37	
ATOM	1696 CB SER 428	7.636 15.393 70.633 1.00 18.11	
ATOM	1697 OG SER 428	7.745 16.794 70.876 1.00 19.14	
ATOM	1698 C SER 428	7.377 15.138 73.154 1.00 18.08	
ATOM	1699 O SER 428	7.968 15.916 73.928 1.00 16.98	
ATOM	1700 N LEU 429	6.134 14.741 73.425 1.00 18.84	
ATOM	1701 CA LEU 429	5.518 15.249 74.633 1.00 19.23	
ATOM	1702 CB LEU 429	4.054 14.807 74.723 1.00 22.17	
ATOM	1703 CG LEU 429	3.187 15.432 73.625 1.00 25.96	
ATOM	1704 CD1 LEU 429	1.800 14.809 73.624 1.00 28.92	
ATOM	1705 CD2 LEU 429	3.087 16.943 73.855 1.00 29.57	
ATOM	1706 C LEU 429	6.296 14.782 75.860 1.00 17.99	
ATOM	1707 O LEU 429	6.465 15.527 76.816 1.00 18.52	
ATOM	1708 N LYS 430	6.778 13.544 75.830 1.00 18.39	
ATOM	1709 CA LYS 430	7.540 13.047 76.957 1.00 17.66	
ATOM	1710 CB LYS 430	7.780 11.544 76.826 1.00 19.73	
ATOM	1711 CG LYS 430	8.539 10.975 78.020 1.00 23.74	
ATOM	1712 CD LYS 430	7.625 11.004 79.260 1.00 27.95	
ATOM	1713 CE LYS 430	8.192 10.194 80.414 1.00 34.36	
ATOM	1714 NZ LYS 430	7.167 10.122 81.490 1.00 36.64	
ATOM	1715 C LYS 430	8.865 13.795 77.077 1.00 18.37	
ATOM	1716 O LYS 430	9.346 14.034 78.191 1.00 18.47	
ATOM	1717 N SER 431	9.435 14.174 75.936 0.50 17.09	AC1
ATOM	1718 CA SER 431	10.693 14.931 75.919 0.50 18.08	AC1

AC1

	,
	٥
3	ø
	0
	4
	15
	j
	m
	12
	ā
	-
	Ų
	(SSS)

10

15

2.0

25

30

35

ATOM 1719 CB SER 431 11.102 15.238 74.471 0.50 17.50 AC1 AC1 ATOM 1720 OG SER 431 12.180 16.159 74.413 0.50 19.63 ATOM 1721 C SER 431 10.472 16.244 76.663 0.50 18.02 AC1 11.297 16.668 77.464 0.50 17.75 AC1 ATOM 1722 O SER 431 ATOM 1723 N PHE 432 9.326 16.875 76.415 1.00 17.68 ATOM 1724 CA PHE 432 9.020 18.162 77.057 1.00 17.81 ATOM 1725 CB PHE 432 7.778 18.817 76.425 1.00 18.74 ATOM 1726 CG PHE 432 8.099 19.713 75.249 1.00 17.54 ATOM 1727 CD1 PHE 432 8.649 20.976 75.448 1.00 18.72 7.851 19.290 73.958 1.00 17.78 ATOM 1728 CD2 PHE 432 ATOM 1729 CE1 PHE 432 8.941 21.800 74.351 1.00 18.20 ATOM 1730 CE2 PHE 432 8.135 20.093 72.863 1.00 18.04 8.684 21.358 73.060 1.00 19.15 ATOM 1731 CZ PHE 432 ATOM 1732 C PHE 432 8.817 17.989 78.550 1.00 18.32 ATOM 1733 O PHE 432 9.170 18.872 79.330 1.00 20.66 ATOM 1734 N GLU 433 8.249 16.852 78.964 1.00 17.15 ATOM 1735 CA GLU 433 8.073 16.592 80.382 1.00 20.50 ATOM 1736 CB GLU 433 7.520 15.192 80.613 1.00 19.84 ATOM 1737 CG GLU 433 6.045 15.053 80.320 1.00 27.71 ATOM 1738 CD GLU 433 5.533 13.688 80.744 1.00 31.07 5.964 13.224 81.823 1.00 34.98 ATOM 1739 OE1 GLU 433 ATOM 1740 OE2 GLU 433 4.714 13.094 80.006 1.00 34.76 ATOM 1741 C GLU 433 9.437 16.691 81.052 1.00 19.32 ATOM 1742 O GLU 433 9.574 17.322 82.106 1.00 20.27 ATOM 1743 N HIS 434 10.438 16.059 80.435 1.00 18.45 ATOM 1744 CA HIS 434 11.810 16.086 80.972 1.00 19.10 ATOM 1745 CB HIS 434 12.708 15.091 80.247 1.00 20.67 ATOM 1746 CG HIS 434 12.346 13.662 80.495 1.00 21.88 ATOM 1747 CD2 HIS 434 12.196 12.621 79.642 1.00 22.64 ATOM 1748 ND1 HIS 434 12.153 13.151 81.763 1.00 24.64 ATOM 1749 CE1 HIS 434 11.901 11.857 81.678 1.00 26.38 ATOM 1750 NE2 HIS 434 11.924 11.509 80.403 1.00 25.49 ATOM 1751 C HIS 434 12.448 17.471 80.900 1.00 19.47 ATOM 1752 O HIS 434 13.029 17.930 81.868 1.00 20.51 ATOM 1753 N LEU 435 12.360 18.122 79.749 1.00 17.30 ATOM 1754 CA LEU 435 12.926 19.464 79.614 1.00 17.70

10

15

20

25

30

35

ATOM 1755 CB LEU 435 12.660 20.017 78.219 1.00 17.54 ATOM 1756 CG LEU 435 13.350 19.239 77.100 1.00 17.06 ATOM 1757 CD1 LEU 435 12.933 19.793 75.764 1.00 19.34 ATOM 1758 CD2 LEU 435 14.874 19.343 77.242 1.00 19.09 ATOM 1759 C LEU 435 12.334 20.411 80.653 1.00 17.96 ATOM 1760 O LEU 435 13.034 21.260 81.193 1.00 18.73 ATOM 1761 N PHE 436 11.035 20.302 80.921 1.00 17.35 ATOM 1762 CA PHE 436 10.460 21.192 81.936 1.00 18.85 ATOM 1763 CB PHE 436 8 920 21 188 81 897 1 00 19 91 ATOM 1764 CG PHE 436 8.340 21.916 80.720 1.00 22.43 ATOM 1765 CD1 PHE 436 8.885 23.113 80.288 1.00 23.77 7.243 21.399 80.040 1.00 23.20 ATOM 1766 CD2 PHE 436 ATOM 1767 CE1 PHE 436 8.353 23.783 79.202 1.00 25.60 ATOM 1768 CE2 PHE 436 6.703 22.063 78.942 1.00 22.41 7.250 23.249 78.521 1.00 26.06 ATOM 1769 CZ PHE 436 ATOM 1770 C PHE 436 10.916 20.802 83.332 1.00 20.10 ATOM 1771 O PHE 436 11.195 21.670 84.161 1.00 22.89 ATOM 1772 N PHE 437 11.001 19.500 83.605 1.00 19.98 ATOM 1773 CA PHE 437 11.412 19.023 84.922 1.00 21.11 ATOM 1774 CB PHE 437 11.364 17.484 84.974 1.00 21.57 ATOM 1775 CG PHE 437 11.628 16.913 86.339 1.00 25.91 ATOM 1776 CD1 PHE 437 10.633 16.924 87.313 1.00 27.17 ATOM 1777 CD2 PHE 437 12.881 16.419 86.665 1.00 27.22 10.891 16.447 88.599 1.00 30.66 ATOM 1778 CE1 PHE 437 ATOM 1779 CE2 PHE 437 13 153 15 942 87 944 1 00 31 40 ATOM 1780 CZ PHE 437 12.158 15.957 88.910 1.00 29.78 ATOM 1781 C PHE 437 12.807 19.496 85.305 1.00 22.67 ATOM 1782 O PHE 437 13.046 19.895 86.464 1.00 24.17 ATOM 1783 N PHE 438 13.724 19.453 84.346 1.00 19.58 ATOM 1784 CA PHE 438 15.103 19.888 84.567 1.00 22.15 ATOM 1785 CB PHE 438 16.038 19.027 83.718 1.00 22.90 ATOM 1786 CG PHE 438 16.093 17.595 84.171 1.00 23.82 ATOM 1787 CD1 PHE 438 16.725 17.262 85.361 1.00 24.00 ATOM 1788 CD2 PHE 438 15.509 16.584 83.419 1.00 27.39 ATOM 1789 CE1 PHE 438 16.773 15.942 85.795 1.00 25.11 ATOM 1790 CE2 PHE 438 15.557 15.253 83.847 1.00 27.37

10

15

2.0

2.5

30

35

16.188 14.935 85.033 1.00 27.90 ATOM 1791 CZ PHE 438 15,334 21,383 84,256 1,00 21,04 ATOM 1792 C PHE 438 ATOM 1793 O PHE 438 16.454 21.875 84.352 1.00 22.98 ATOM 1794 N HIS 439 14.267 22.077 83.867 1.00 19.84 ATOM 1795 CA HIS 439 14 311 23 503 83 508 1.00 19 79 14.550 24.380 84.742 1.00 21.68 ATOM 1796 CB HIS 439 ATOM 1797 CG HIS 439 13.463 24.294 85.763 1.00 24.96 ATOM 1798 CD2 HIS 439 12.345 25.037 85.939 1.00 27.66 ATOM 1799 ND1 HIS 439 13.440 23.331 86.747 1.00 26.44 12.353 23.481 87.481 1.00 27.37 ATOM 1800 CE1 HIS 439 ATOM 1801 NE2 HIS 439 11.672 24.511 87.012 1.00 28.08 ATOM 1802 C HIS 439 15.375 23.803 82.469 1.00 20.93 16.185 24.726 82.626 1.00 23.42 ATOM 1803 O HIS 439 15 318 23 068 81 366 1.00 16.51 ATOM 1804 N LEU 440 ATOM 1805 CA LEU 440 16.289 23.200 80.301 1.00 18.97 ATOM 1806 CB LEU 440 16.820 21.813 79.917 1.00 19.31 17.585 21.101 81.017 1.00 21.82 ATOM 1807 CG LEU 440 ATOM 1808 CD1 LEU 440 17,920 19,672 80,567 1,00 24,43 ATOM 1809 CD2 LEU 440 18.839 21.874 81.341 1.00 21.97 ATOM 1810 C LEU 440 15.751 23.859 79.042 1.00 20.05 16.497 24.030 78.099 1.00 21.82 ATOM 1811 O LEU 440 14.478 24.229 79.038 1.00 19.87 ATOM 1812 N VAL 441 ATOM 1813 CA VAL 441 13.879 24.814 77.833 1.00 21.84 ATOM 1814 CB VAL 441 12.795 23.830 77.247 1.00 22.63 ATOM 1815 CG1 VAL 441 11.601 23.713 78.192 1.00 22.79 12.365 24.276 75.855 1.00 24.87 ATOM 1816 CG2 VAL 441 ATOM 1817 C VAL 441 13.306 26.224 78.045 1.00 22.01 ATOM 1818 O VAL 441 12.587 26.478 79.009 1.00 20.37 ATOM 1819 N ALA 442 13.646 27.122 77.120 1.00 23.96 13.233 28.529 77.172 1.00 27.08 ATOM 1820 CA ALA 442 ATOM 1821 CB ALA 442 14.246 29.393 76.392 1.00 28.21 ATOM 1822 C ALA 442 11.846 28.718 76.591 1.00 28.96 ATOM 1823 O ALA 442 11.655 29.494 75.658 1.00 30.12 ATOM 1824 N ASP 443 10.895 28.011 77.178 1.00 30.46 9.493 27.994 76.764 1.00 31.83 ATOM 1825 CA ASP 443 ATOM 1826 CB ASP 443 8.678 27.367 77.906 1.00 33.17

10

15

20

25

30

35

ATOM 1827 CG ASP 443 7.208 27.218 77.581 1.00 34.98 ATOM 1828 OD1 ASP 443 6.856 26.945 76.404 1.00 37.47 ATOM 1829 OD2 ASP 443 6.404 27.346 78.524 1.00 31.58 ATOM 1830 C ASP 443 8.873 29.320 76.318 1.00 31.97 ATOM 1831 O ASP 443 8.426 29.453 75.180 1.00 30.41 ATOM 1832 N THR 444 8.854 30.304 77.205 1.00 32.53 ATOM 1833 CA THR 444 8.236 31.586 76.891 1.00 32.98 ATOM 1834 CB THR 444 7.965 32.371 78.198 1.00 34.53 ATOM 1835 OG1 THR 444 9.196 32.581 78.900 1.00 37.04 ATOM 1836 CG2 THR 444 7.020 31.577 79.102 1.00 35.95 ATOM 1837 C THR 444 8.981 32.486 75.901 1.00 32.99 ATOM 1838 O THR 444 8,399 33.436 75.370 1.00 32.71 ATOM 1839 N SER 445 10.248 32.179 75.639 1.00 30.56 ATOM 1840 CA SER 445 11.071 32.977 74.727 1.00 29.90 ATOM 1841 CB SER 445 12.481 33.132 75.313 1.00 29.52 ATOM 1842 OG SER 445 12.418 33.766 76.576 1.00 31.76 ATOM 1843 C SER 445 11,199 32,429 73,308 1,00 29,39 ATOM 1844 O SER 445 11.580 33.153 72.387 1.00 28.30 10.875 31.151 73.133 1.00 26.98 ATOM 1845 N ILE 446 ATOM 1846 CA ILE 446 11.010 30.511 71.840 1.00 25.95 ATOM 1847 CB ILE 446 10.656 29.013 71.961 1.00 26.36 ATOM 1848 CG2 ILE 446 10.295 28.431 70.595 1.00 24.39 ATOM 1849 CG1 ILE 446 11.864 28.300 72.575 1.00 27.57 ATOM 1850 CD1 ILE 446 11 637 26 869 72 971 1 00 27 13 ATOM 1851 C ILE 446 10.312 31.144 70.640 1.00 25.28 ATOM 1852 O ILE 446 10.917 31.247 69.571 1.00 23.47 ATOM 1853 N ALA 447 9.058 31.549 70.809 1.00 26.37 8.316 32.183 69.725 1.00 28.80 ATOM 1854 CA ALA 447 ATOM 1855 CB ALA 447 6.932 32.606 70.219 1.00 30.52 ATOM 1856 C ALA 447 9.114 33.394 69.218 1.00 28.51 ATOM 1857 O ALA 447 9.229 33.608 68.005 1.00 29.41 ATOM 1858 N GLY 448 9.675 34.164 70.155 1.00 28.53 ATOM 1859 CA GLY 448 10.474 35.337 69.811 1.00 27.89 ATOM 1860 C GLY 448 11.762 34.993 69.095 1.00 28.77 ATOM 1861 O GLY 448 12,167 35,692 68,162 1,00 28,23 ATOM 1862 N TYR 449 12.435 33.927 69.536 1.00 27.26

jen.
10
V.
O
40
UM
U
J
se
1
TU
Link

10

15

20

25

30

35

ATOM 1863 CA TYR 449 13.666 33.502 68.872 1.00 28.14 ATOM 1864 CB TYR 449 14.262 32.267 69.553 1.00 26.16 ATOM 1865 CG TYR 449 14.683 32.492 70.990 1.00 28.82 ATOM 1866 CD1 TYR 449 14.913 33.782 71.482 1.00 29.84 ATOM 1867 CE1 TYR 449 15.336 33.988 72.802 1.00 32.66 ATOM 1868 CD2 TYR 449 14.881 31.412 71.853 1.00 29.90 ATOM 1869 CE2 TYR 449 15.306 31.604 73.173 1.00 30.71 ATOM 1870 CZ TYR 449 15.532 32.887 73.641 1.00 32.74 ATOM 1871 OH TYR 449 15.979 33.070 74.939 1.00 36.98 ATOM 1872 C TYR 449 13.361 33.150 67.420 1.00 27.51 ATOM 1873 O TYR 449 14.116 33.491 66.513 1.00 27.99 ATOM 1874 N ILE 450 12.254 32.442 67.207 1.00 27.41 ATOM 1875 CA ILE 450 11.876 32.053 65.861 1.00 27.70 ATOM 1876 CB ILE 450 10.662 31.102 65.863 1.00 26.64 ATOM 1877 CG2 ILE 450 10.292 30.744 64.413 1.00 26.88 ATOM 1878 CG1 ILE 450 11.003 29.846 66.690 1.00 27.46 ATOM 1879 CD1 ILE 450 9.811 28.956 67.032 1.00 24.45 ATOM 1880 C ILE 450 11.534 33.295 65.041 1.00 29.34 ATOM 1881 O ILE 450 11.994 33.440 63.911 1.00 30.32 ATOM 1882 N ARG 451 10.735 34.187 65.617 1.00 30.43 ATOM 1883 CA ARG 451 10.351 35.416 64.923 1.00 33.00 ATOM 1884 CB ARG 451 9.514 36.306 65.851 1.00 32.56 ATOM 1885 CG ARG 451 8.874 37.519 65.161 1.00 34.91 ATOM 1886 CD ARG 451 7.955 38.328 66.076 1.00 36.14 ATOM 1887 NE ARG 451 6.768 37.599 66.518 1.00 37.46 ATOM 1888 CZ ARG 451 6.669 36.943 67.672 1.00 40.02 ATOM 1889 NH1 ARG 451 7.690 36.921 68.521 1.00 41.16 ATOM 1890 NH2 ARG 451 5.547 36.299 67.976 1.00 40.59 ATOM 1891 C ARG 451 11.629 36.138 64.472 1.00 34.57 ATOM 1892 O ARG 451 11.761 36.516 63.298 1.00 34.59 ATOM 1893 N ASP 452 12.578 36.304 65.392 1.00 36.05 ATOM 1894 CA ASP 452 13.837 36.975 65.070 1.00 39.88 ATOM 1895 CB ASP 452 14.690 37.184 66.331 1.00 42.41 ATOM 1896 CG ASP 452 14.004 38.065 67.364 1.00 46.01 ATOM 1897 OD1 ASP 452 13.162 38.897 66.961 1.00 46.57 ATOM 1898 OD2 ASP 452 14.315 37.934 68.576 1.00 48.55

10

15

20

25

30

35

ATOM 1899 C ASP 452 14.657 36.212 64.039 1.00 40.80 ATOM 1900 O ASP 452 15.219 36.805 63.112 1.00 42.52 ATOM 1901 N ALA 453 14,730 34,896 64,197 1,00 41,16 ATOM 1902 CA ALA 453 15.493 34.071 63.272 1.00 42.41 ATOM 1903 CB ALA 453 15.585 32.643 63.796 1.00 41.71 ATOM 1904 C ALA 453 14.904 34.070 61.863 1.00 44.06 ATOM 1905 O ALA 453 15.635 33.910 60.887 1.00 44.96 ATOM 1906 N LEU 454 13.590 34.259 61.759 1.00 45.34 12 921 34 261 60 460 1.00 47.12 ATOM 1907 CA LEU 454 ATOM 1908 CB LEU 454 11.419 33.989 60.631 1.00 42.61 11.078 32.514 60.884 1.00 38.89 ATOM 1909 CG LEU 454 ATOM 1910 CD1 LEU 454 9 576 32 329 60 950 1 00 36 29 ATOM 1911 CD2 LEU 454 11.660 31.657 59.764 1.00 36.23 ATOM 1912 C LEU 454 13.149 35.544 59.669 1.00 50.37 13.255 35.506 58.443 1.00 51.61 ATOM 1913 O LEU 454 ATOM 1914 N ARG 455 13.218 36.679 60.360 1.00 54.48 ATOM 1915 CA ARG 455 13.486 37.951 59.688 1.00 58.31 ATOM 1916 CB ARG 455 13.128 39.147 60.582 1.00 59.22 ATOM 1917 CG ARG 455 11.635 39.352 60.806 1.00 60.97 11.318 40.787 61.228 1.00 62.50 ATOM 1918 CD ARG 455 ATOM 1919 NE ARG 455 10.998 40.919 62.648 1.00 64.04 11.873 40.784 63.640 1.00 64.71 ATOM 1920 CZ ARG 455 ATOM 1921 NH1 ARG 455 13.146 40.511 63.378 1.00 64.92 ATOM 1922 NH2 ARG 455 11.470 40.923 64.897 1.00 64.48 ATOM 1923 C ARG 455 14 988 37 938 59 452 1.00 60 72 ATOM 1924 O ARG 455 15.597 38.964 59.147 1.00 61.55 ATOM 1925 N ASN 456 15.557 36.743 59.597 1.00 63.01 16.983 36.482 59.463 1.00 64.82 ATOM 1926 CA ASN 456 17.434 36.512 57.987 1.00 66.21 ATOM 1927 CB ASN 456 ATOM 1928 CG ASN 456 17.254 37.871 57.327 1.00 67.51 ATOM 1929 OD1 ASN 456 17.901 38.850 57.702 1.00 68.69 ATOM 1930 ND2 ASN 456 16.377 37.930 56.326 1.00 68.01 17.795 37.442 60.317 1.00 65.37 ATOM 1931 C ASN 456 ATOM 1932 O ASN 456 17.456 37.680 61.480 1.00 65.63 ATOM 1933 N GLY 457 18.858 37.997 59.749 1.00 65.99 ATOM 1934 CA GLY 457 19.704 38.896 60.510 1.00 66.46

10

15

20

25

30

35

ATOM 1935 C GLY 457 20.739 38.015 61.176 1.00 66.78 ATOM 1936 O GLY 457 21,568 38,471 61,968 1,00 67,21 ATOM 1937 N GLY 458 20.669 36.728 60.844 1.00 66.86 ATOM 1938 CA GLY 458 21.594 35.753 61.384 1.00 66.84 ATOM 1939 C GLY 458 22.018 34.761 60.315 1.00 66.86 ATOM 1940 O GLY 458 21.450 34.801 59.199 1.00 66.65 ATOM 1941 OXT GLY 458 22.922 33.943 60.593 1.00 65.49 ATOM 1942 OH2 TIP 1003 30.252 23.128 74.386 1.00 27.69 ATOM 1943 OH2 TIP 1005 14.203 25.558 89.644 1.00 25.22 ATOM 1944 OH2 TIP 1006 8.388 25.042 72.262 1.00 22.81 ATOM 1945 OH2 TIP 1008 8.367 21.538 69.460 1.00 19.23 ATOM 1946 OH2 TIP 1009 -7.350 22.030 52.884 1.00 80.11 -4.017 19.644 67.897 1.00 33.26 ATOM 1947 OH2 TIP 1010 ATOM 1948 OH2 TIP 1011 8.365 3.022 77.974 1.00 47.93 ATOM 1949 OH2 TIP 1012 30.690 8.779 67.839 1.00 26.30 ATOM 1950 OH2 TIP 1013 12.264 8.843 80.249 1.00 26.01 ATOM 1951 OH2 TIP 1014 -1.764 16.382 62.652 1.00 44.82 ATOM 1952 OH2 TIP 1015 20.301 34.946 75.498 1.00 51.92 ATOM 1953 OH2 TIP 1016 14.443 15.693 61.296 1.00 22.04 ATOM 1954 OH2 TIP 1017 12.487 31.635 78.951 1.00 36.76 ATOM 1955 OH2 TIP 1018 16.579 6.557 83.739 1.00 27.86 ATOM 1956 OH2 TIP 1019 -0.626 26.615 50.499 1.00 30.82 ATOM 1957 OH2 TIP 1021 3.543 20.127 64.859 1.00 23.80 ATOM 1958 OH2 TIP 1022 4.772 0.996 47.855 1.00 40.67 ATOM 1959 OH2 TIP 1023 9.799 29.451 51.621 1.00 30.93 ATOM 1960 OH2 TIP 1024 7.476 19.030 68.589 1.00 22.30 ATOM 1961 OH2 TIP 1025 20.355 7.131 58.551 1.00 52.44 ATOM 1962 OH2 TIP 1026 -0.829 29.526 57.153 1.00 31.90 ATOM 1963 OH2 TIP 1027 11.560 -6.342 53.442 1.00 52.29 15.278 0.625 72.808 1.00 27.12 ATOM 1964 OH2 TIP 1028 ATOM 1965 OH2 TIP 1029 22,593 26,832 76,012 1,00 35,56 ATOM 1966 OH2 TIP 1031 3.001 25.878 68.078 1.00 22.76 ATOM 1967 OH2 TIP 1032 13.489 25.800 47.958 1.00 47.50 ATOM 1968 OH2 TIP 1033 -7.554 18.088 60.905 1.00 30.53 ATOM 1969 OH2 TIP 1034 24.742 18.595 64.446 1.00 44.88 ATOM 1970 OH2 TIP 1035 13.751 37.059 78.800 1.00 60.77

10

15

20

2.5

30

35

ATOM 1971 OH2 TIP 1036 -0.515 10.167 75.163 1.00 36.51 ATOM 1972 OH2 TIP 1037 12.373 35.911 72.901 1.00 32.65 ATOM 1973 OH2 TIP 1039 23.543 26.270 78.523 1.00 24.40 ATOM 1974 OH2 TIP 1040 17.896 20.961 59.259 1.00 39.57 ATOM 1975 OH2 TIP 1041 8.248 15.187 89.930 1.00 59.85 7.418 31.128 73.133 1.00 34.33 ATOM 1976 OH2 TIP 1042 21.123 8.890 53.894 1.00 67.39 ATOM 1977 OH2 TIP 1043 ATOM 1978 OH2 TIP 1045 15.162 18.243 53.355 1.00 28.26 ATOM 1979 OH2 TIP 1050 4.216 23.224 44.827 1.00 46.56 ATOM 1980 OH2 TIP 1051 17 523 1.262 73.909 1.00 23.12 -0.169 20.149 67.166 1.00 67.45 ATOM 1981 OH2 TIP 1052 ATOM 1982 OH2 TIP 1053 20.135 12.837 55.866 1.00 51.70 10.612 35.387 77.215 1.00 57.20 ATOM 1983 OH2 TIP 1054 ATOM 1984 OH2 TIP 1055 14.587 38.805 73.912 1.00 56.14 22.658 15.094 55.769 1.00 63.46 ATOM 1985 OH2 TIP 1056 ATOM 1986 OH2 TIP 1057 8.196 1.415 39.058 1.00 55.65 ATOM 1987 OH2 TIP 1058 10.807 2.725 77.173 1.00 22.15 ATOM 1988 OH2 TIP 1059 19.013 20.604 62.130 1.00 32.43 2.388 16.861 45.084 1.00 25.70 ATOM 1989 OH2 TIP 1061 ATOM 1990 OH2 TIP 1063 5.229 6.816 86.424 1.00 59.99 ATOM 1991 OH2 TIP 1501 18.919 15.965 66.146 1.00 24.36 ATOM 1992 OH2 TIP 1502 2,744 33,258 66,246 1,00 30,10 ATOM 1993 OH2 TIP 1503 4.527 17.244 77.877 1.00 23.98 ATOM 1994 OH2 TIP 1504 -0.815 22.723 68.903 1.00 24.06 ATOM 1995 OH2 TIP 1506 22.697 1.204 69.760 1.00 28.71 ATOM 1996 OH2 TIP 1507 12.438 25.185 81.547 1.00 28.20 ATOM 1997 OH2 TIP 1508 17.107 31.275 76.636 1.00 33.34 ATOM 1998 OH2 TIP 1509 17.900 15.686 59.270 1.00 37.88 7 197 12 183 44 002 1 00 29 62 ATOM 1999 OH2 TIP 1510 ATOM 2000 OH2 TIP 1511 -4.834 15.832 60.463 1.00 33.76 ATOM 2001 OH2 TIP 1512 11.093 1.186 74.736 1.00 29.08 ATOM 2002 OH2 TIP 1513 -0.145 2.568 51.845 1.00 30.78 ATOM 2003 OH2 TIP 1514 -6.100 23.488 73.541 1.00 27.96 ATOM 2004 OH2 TIP 1515 8.298 14.512 44.198 1.00 34.89 ATOM 2005 OH2 TIP 1516 0.418 26.098 68.989 1.00 28.71 ATOM 2006 OH2 TIP 1517 -7.177 16.116 59.030 1.00 32.04

10

15

2.0

2.5

30

35

18.000 18.387 62.314 1.00 32.49 ATOM 2007 OH2 TIP 1519 ATOM 2008 OH2 TIP 1520 21,777 20,403 61,898 1.00 38,66 ATOM 2009 OH2 TIP 1521 -1.379 32.714 63.883 1.00 40.86 ATOM 2010 OH2 TIP 1522 1 931 22 610 68 721 1.00 31.49 ATOM 2011 OH2 TIP 1523 -3.158 9.157 64.790 1.00 46.08 2.081 4.709 65.432 1.00 38.87 ATOM 2012 OH2 TIP 1524 ATOM 2013 OH2 TIP 1525 3.829 11.325 75.940 1.00 34.36 21.845 33.747 71.839 1.00 51.86 ATOM 2014 OH2 TIP 1527 ATOM 2015 OH2 TIP 1528 12.196 0.941 78.760 1.00 46.53 30.316 21.478 85.009 1.00 28.49 ATOM 2016 OH2 TIP 1529 ATOM 2017 OH2 TIP 1530 9.786 2.798 91.182 1.00 58.36 ATOM 2018 OH2 TIP 1531 16.571 8.007 48.772 1.00 38.32 3.764 24.595 70.409 1.00 31.40 ATOM 2019 OH2 TIP 1532 -0.952 5.111 57.996 1.00 39.42 ATOM 2020 OH2 TIP 1533 ATOM 2021 OH2 TIP 1534 8.395 29.793 48.733 1.00 45.92 18.190 -0.943 54.382 1.00 55.57 ATOM 2022 OH2 TIP 1535 4.583 13.859 64.203 1.00 30.44 ATOM 2023 OH2 TIP 1536 ATOM 2024 OH2 TIP 1538 12.012 14.232 84.365 1.00 33.97 ATOM 2025 OH2 TIP 1539 -1.284 36.017 69.736 1.00 57.91 ATOM 2026 OH2 TIP 1540 2.454 15.898 79.022 1.00 40.22 2.719 2.670 49.088 1.00 32.00 ATOM 2027 OH2 TIP 1544 ATOM 2028 OH2 TIP 1545 13.537 37.410 71.136 1.00 41.29 ATOM 2029 OH2 TIP 1546 22.697 0.071 79.248 1.00 32.01 ATOM 2030 OH2 TIP 1548 -0.239 7.542 39.851 1.00 52.37 0.076 10.603 44.453 1.00 41.67 ATOM 2031 OH2 TIP 1549 ATOM 2032 OH2 TIP 1550 31.157 3.039 59.611 1.00 43.66 ATOM 2033 OH2 TIP 1551 4.226 34.045 72.549 1.00 53.58 ATOM 2034 OH2 TIP 1554 10.022 33.359 56.088 1.00 41.48 ATOM 2035 OH2 TIP 1555 -1.058 37.708 61.917 1.00 54.81 ATOM 2036 OH2 TIP 1556 -4 583 15 870 53.480 1.00 37.02 ATOM 2037 OH2 TIP 1557 23.851 8.517 92.595 1.00 36.91 ATOM 2038 OH2 TIP 1558 -7.204 28.744 59.955 1.00 35.72 19.483 16.334 88.331 1.00 34.61 ATOM 2039 OH2 TIP 1560 ATOM 2040 OH2 TIP 1561 1.968 8.086 38.648 1.00 57.90 ATOM 2041 OH2 TIP 1562 32.430 -4.459 71.625 1.00 63.22 ATOM 2042 OH2 TIP 1563 7.819 12.682 83.368 1.00 47.71

10

15

20

25

30

35

ATOM 2043 OH2 TIP 1564 -5.435 18.376 72.810 1.00 41.90 ATOM 2044 OH2 TIP 1565 19.550 17.394 63.917 1.00 31.79 ATOM 2045 OH2 TIP 1566 24.069 28.502 85.703 1.00 50.24 ATOM 2046 OH2 TIP 1568 26.854 12.830 56.392 1.00 51.68 ATOM 2047 OH2 TIP 1570 3.595 32.325 68.760 1.00 45.07 ATOM 2048 OH2 TIP 1571 24,805 8,300 62,036 1,00 28,27 ATOM 2049 OH2 TIP 1572 4.194 17.554 63.640 1.00 26.21 ATOM 2050 OH2 TIP 1573 2.589 20.195 67.352 1.00 34.52 ATOM 2051 OH2 TIP 1574 15.713 17.937 61.017 1.00 52.03 ATOM 2052 OH2 TIP 1575 -9.321 14.210 59.772 1.00 33.92 ATOM 2053 OH2 TIP 1576 13.215 7.332 82.542 1.00 31.45 10.470 24.539 83.194 1.00 35.29 ATOM 2054 OH2 TIP 1577 ATOM 2055 OH2 TIP 1578 25,712 17,999 53,496 1,00 41,46 ATOM 2056 OH2 TIP 1579 9.445 -0.239 41.882 1.00 41.51 ATOM 2057 OH2 TIP 1580 6.603 16.005 42.611 1.00 32.35 ATOM 2058 OH2 TIP 1581 -1.523 7.654 59.739 1.00 50.11 ATOM 2059 OH2 TIP 1582 8.397 34.515 72.891 1.00 33.81 ATOM 2060 OH2 TIP 1583 2.742 39.191 60.949 1.00 39.77 ATOM 2061 OH2 TIP 1584 18.933 6.009 52.002 1.00 45.27 ATOM 2062 OH2 TIP 1585 -1.653 20.171 69.665 1.00 37.15 ATOM 2063 OH2 TIP 1586 -2.633 4.655 52.475 1.00 49.05 ATOM 2064 OH2 TIP 1587 36.297 28.180 83.444 1.00 41.56 ATOM 2065 OH2 TIP 1588 -0.851 31.806 55.808 1.00 34.41 ATOM 2066 OH2 TIP 1589 4.002 34.625 70.007 1.00 46.13 ATOM 2067 OH2 TIP 1590 32.711 20.152 84.581 1.00 53.56 ATOM 2068 OH2 TIP 1591 19.998 6.099 87.630 1.00 31.12 ATOM 2069 OH2 TIP 1593 -0.189 3.637 35.682 1.00 54.58 ATOM 2070 OH2 TIP 1594 12.455 12.705 39.358 1.00 55.12 ATOM 2071 OH2 TIP 1596 -2.554 -6.074 47.925 1.00 55.01 ATOM 2072 OH2 TIP 1597 5.017 28.176 75.017 1.00 42.02 ATOM 2073 OH2 TIP 1598 28.617 32.433 80.891 1.00 65.40 ATOM 2074 OH2 TIP 1599 8.680 7.258 78.481 1.00 52.56 ATOM 2075 OH2 TIP 1600 18.188 12.950 87.437 1.00 47.03 ATOM 2076 OH2 TIP 1601 -11.532 19.931 55.756 1.00 48.92 ATOM 2077 OH2 TIP 1602 22.073 14.215 52.571 1.00 49.32 ATOM 2078 OH2 TIP 1603 -3.860 34.262 53.170 1.00 48.97

10

15

20

25

30

35

1.118 10.847 82.180 1.00 44.11 ATOM 2079 OH2 TIP 1604 19.335 32.031 77.782 1.00 48.61 ATOM 2080 OH2 TIP 1605 ATOM 2081 OH2 TIP 1606 19.174 9.955 48.654 1.00 40.42 ATOM 2082 OH2 TIP 1607 23.632 -1.631 71.300 1.00 37.97 ATOM 2083 OH2 TIP 1608 26.622 26.695 85.361 1.00 44.14 ATOM 2084 OH2 TIP 1609 22 586 -1.769 57.526 1.00 48.15 ATOM 2085 OH2 TIP 1610 21.977 5.567 60.712 1.00 37.76 ATOM 2086 OH2 TIP 1611 21.634 2.725 67.903 1.00 41.42 ATOM 2087 OH2 TIP 1612 4.046 4.187 75.513 1.00 55.86 0.807 25.979 47.960 1.00 38.30 ATOM 2088 OH2 TIP 1614 17.333 37.351 72.160 1.00 55.70 ATOM 2089 OH2 TIP 1615 2.475 15.902 62.566 1.00 38.40 ATOM 2090 OH2 TIP 1616 ATOM 2091 OH2 TIP 1618 0.658 14.983 64.592 1.00 60.57 ATOM 2092 OH2 TIP 1619 -6.509 17.844 52.643 1.00 41.17 27 000 -1.287 80.946 1.00 51.49 ATOM 2093 OH2 TIP 1621 ATOM 2094 OH2 TIP 1622 3,271 9,154 86,392 1.00 55.17 3,433 19,409 44,225 1.00 50.54 ATOM 2095 OH2 TIP 1627 ATOM 2096 OH2 TIP 1628 2.390 26.629 72.360 1.00 42.60 9.893 39.104 69.833 1.00 54.40 ATOM 2097 OH2 TIP 1629 ATOM 2098 OH2 TIP 1630 2.709 14.153 43.455 1.00 34.37 ATOM 2099 OH2 TIP 1631 11.049 12.448 88.232 1.00 45.81 4.576 31.506 72.757 1.00 39.34 ATOM 2100 OH2 TIP 1632 ATOM 2101 OH2 TIP 1634 6.784 36.285 71.148 1.00 51.53 6.667 43.335 56.568 1.00 51.21 ATOM 2102 OH2 TIP 1635 ATOM 2103 OH2 TIP 1636 -5.771 9.260 60.442 1.00 44.79 ATOM 2104 OH2 TIP 1638 0.052 33.418 66.937 1.00 47.03 ATOM 2105 OH2 TIP 1641 0.354 1.055 46.133 1.00 54.03 ATOM 2106 OH2 TIP 1642 24.406 30.113 88.300 1.00 48.82 26.619 20.182 66.495 1.00 38.01 ATOM 2107 OH2 TIP 1643 ATOM 2108 OH2 TIP 1644 17.492 7.024 42.815 1.00 65.02 ATOM 2109 OH2 TIP 1645 25.942 26.481 82.676 1.00 49.52 ATOM 2110 OH2 TIP 1646 20.601 16.199 68.672 1.00 37.35 ATOM 2111 OH2 TIP 1649 27.616 9.156 63.460 1.00 37.92 ATOM 2112 OH2 TIP 1650 0.428 -3.038 44.190 1.00 54.50 ATOM 2113 OH2 TIP 1652 -7.028 20.462 59.299 1.00 33.58 ATOM 2114 OH2 TIP 1653 -2.848 32.314 67.354 1.00 49.02

10

15

20

25

30

35

-0.686 17.762 66.362 1.00 46.03 ATOM 2115 OH2 TIP 1654 ATOM 2116 OH2 TIP 1655 19.583 17.275 60.162 1.00 41.00 ATOM 2117 OH2 TIP 1656 13.719 36.618 75.139 1.00 51.89 9.386 -0.422 71.399 1.00 43.15 ATOM 2118 OH2 TIP 1657 ATOM 2119 OH2 TIP 1659 23 690 28 880 79 578 1.00 42 62 22.069 3.800 58.682 1.00 46.06 ATOM 2120 OH2 TIP 1660 ATOM 2121 OH2 TIP 1661 20.671 13.353 58.841 1.00 57.05 27.473 10.135 82.332 1.00 47.43 ATOM 2122 OH2 TIP 1662 ATOM 2123 OH2 TIP 1664 9.564 26.542 84.601 1.00 44.55 29.122 9.606 65.764 1.00 45.20 ATOM 2124 OH2 TIP 1666 ATOM 2125 OH2 TIP 1668 13.135 20.507 41.865 1.00 59.09 ATOM 2126 OH2 TIP 1669 22.639 11.672 58.999 1.00 54.98 -1.845 6.027 76.197 1.00 48.89 ATOM 2127 OH2 TIP 1670 ATOM 2128 OH2 TIP 1672 4 883 25 252 42 734 1 00 51.13 1.329 39.322 66.763 1.00 68.30 ATOM 2129 OH2 TIP 1675 ATOM 2130 OH2 TIP 1676 12.783 29.313 87.079 1.00 54.62 ATOM 2131 OH2 TIP 1679 25.035 18.339 57.364 1.00 54.53 ATOM 2132 OH2 TIP 1682 29.392 -1.856 57.721 1.00 37.30 ATOM 2133 OH2 TIP 1683 28.780 9.970 58.622 1.00 54.22 ATOM 2134 OH2 TIP 1685 4.741 39.274 62.499 1.00 46.58 -3.084 6.977 49.478 1.00 57.17 ATOM 2135 OH2 TIP 1686 ATOM 2136 OH2 TIP 1687 26.519 30.868 83.197 1.00 64.53 ATOM 2137 OH2 TIP 1688 -2.784 37.278 67.289 1.00 59.53 ATOM 2138 OH2 TIP 1689 18.691 10.604 88.296 1.00 52.44 27.919 6.703 82.226 1.00 44.84 ATOM 2139 OH2 TIP 1690 ATOM 2140 OH2 TIP 1691 -4.338 11.103 48.033 1.00 55.91 ATOM 2141 OH2 TIP 1692 -7.853 9.429 46.864 1.00 63.74 10.901 -1.686 67.477 1.00 41.21 ATOM 2142 OH2 TIP 1693 ATOM 2143 OH2 TIP 1694 -2.114 6.315 55.259 1.00 56.21 ATOM 2144 OH2 TIP 1695 17.482 15.932 44.391 1.00 41.18 ATOM 2145 OH2 TIP 1696 -12.326 38.088 61.786 1.00 53.30 ATOM 2146 OH2 TIP 1697 -2.176 40.471 68.230 1.00 68.88 ATOM 2147 OH2 TIP 1700 6.514 -1.974 53.366 1.00 51.67 ATOM 2148 OH2 TIP 1701 21.800 10.610 55.773 1.00 60.93 ATOM 2149 OH2 TIP 1702 3.975 27.046 41.446 1.00 44.88 ATOM 2150 OH2 TIP 1703 26.678 -3.660 64.081 1.00 62.42

10

15

20

25

30

35

ATOM 2151 OH2 TIP 1704 2.958 12.027 86.133 1.00 53.52 ATOM 2152 OH2 TIP 1705 4.264 22.050 63.018 1.00 16.96 ATOM 2153 OH2 TIP 1706 22,999 26,329 63,006 1.00 32,17 ATOM 2154 OH2 TIP 1707 5.614 2.688 68.201 1.00 42.08 ATOM 2155 OH2 TIP 1708 -2.967 17.730 54.394 1.00 38.89 ATOM 2156 OH2 TIP 1709 25.853 10.594 62.118 1.00 43.50 ATOM 2157 OH2 TIP 1711 13.060 12.966 86.563 1.00 41.22 19.784 15.472 45.489 1.00 58.17 ATOM 2158 OH2 TIP 1712 10.567 14.806 42.991 1.00 43.48 ATOM 2159 OH2 TIP 1713 ATOM 2160 OH2 TIP 1714 24.079 30.190 83.477 1.00 47.61 ATOM 2161 OH2 TIP 1715 23.927 21.975 63.464 1.00 44.77 ATOM 2162 OH2 TIP 1716 15.801 20.193 58.769 1.00 34.32 ATOM 2163 OH2 TIP 1717 23.867 27.717 72.712 1.00 40.47 24.567 27.201 69.884 1.00 45.97 ATOM 2164 OH2 TIP 1718 ATOM 2165 OH2 TIP 1719 32.141 -1.375 73.278 1.00 62.31 19.799 24.122 57.454 1.00 35.07 ATOM 2166 OH2 TIP 1720 18.297 23.286 53.598 1.00 43.88 ATOM 2167 OH2 TIP 1721 ATOM 2168 OH2 TIP 1722 8.617 1.105 73.470 1.00 48.55 ATOM 2169 OH2 TIP 1723 28.598 25.728 64.296 1.00 46.24 ATOM 2170 OH2 TIP 1725 19.225 33.547 73.276 1.00 44.07 ATOM 2171 OH2 TIP 1726 1,762 4.546 47.584 1.00 50.27 ATOM 2172 OH2 TIP 1727 10.895 28.774 83.657 1.00 54.87 9.989 36.628 73.713 1.00 46.56 ATOM 2173 OH2 TIP 1728 ATOM 2174 OH2 TIP 1729 -1.331 8.332 70.133 1.00 46.76 ATOM 2175 OH2 TIP 1730 24.262 12.802 55.386 1.00 59.24 28.623 25.788 86.798 1.00 51.87 ATOM 2176 OH2 TIP 1731 ATOM 2177 OH2 TIP 1732 -0.501 4.843 68.521 1.00 47.96 ATOM 2178 OH2 TIP 1736 18.422 4.635 54.793 1.00 51.00 ATOM 2179 OH2 TIP 1737 -5.388 27.319 50.727 1.00 46.53 -2.286 20.842 72.915 1.00 45.95 ATOM 2180 OH2 TIP 1738 0.996 4.268 39.511 1.00 52.67 ATOM 2181 OH2 TIP 1739 ATOM 2182 OH2 TIP 1740 -10.886 28.616 64.116 1.00 45.22 ATOM 2183 OH2 TIP 1741 20.353 -4.883 70.512 1.00 61.31 ATOM 2184 OH2 TIP 1742 22,491 16,164 60,365 1,00 58,19 ATOM 2185 OH2 TIP 3001 15,272 21,419 87,789 1,00 27,44 ATOM 2186 OH2 TIP 3002 13.055 32.876 52.925 1.00 53.35

10

15

20

2.5

30

35

ATOM 2187 OH2 TIP 3006 16.014 18.841 64.083 1.00 56.45 ATOM 2188 OH2 TIP 3008 16.802 30.100 54.388 1.00 48.87 ATOM 2189 OH2 TIP 3009 13.673 27.099 82.740 1.00 32.07 ATOM 2190 OH2 TIP 3010 30.041 24.325 84.969 1.00 41.40 ATOM 2191 OH2 TIP 3007 -2.102 35.612 60.958 1.00 52.05 ATOM 2192 OH2 TIP 3011 7 242 14.501 40.017 1.00 51.46 1.031 36.834 60.593 1.00 49.05 ATOM 2193 OH2 TIP 3012 ATOM 2194 OH2 TIP 3013 0.026 24.244 72.355 1.00 42.35 -7.871 31.986 57.037 1.00 46.09 ATOM 2195 OH2 TIP 3015 ATOM 2196 OH2 TIP 3019 8 655 -3 490 62 423 1.00 44.56 -0.191 30.553 51.677 1.00 54.31 ATOM 2197 OH2 TIP 3020 3.107 37.905 57.599 1.00 48.07 ATOM 2198 OH2 TIP 3023 26.217 6.182 84.277 1.00 47.75 ATOM 2199 OH2 TIP 3024 ATOM 2200 OH2 TIP 3025 2.594 16.520 65.838 1.00 40.67 23.874 12.843 85.264 1.00 42.79 ATOM 2201 C1 EPH 4000 ATOM 2202 C2 EPH 4000 23.099 13.772 86.129 1.00 44.39 24.923 13.000 83.062 1.00 45.55 ATOM 2203 C4 EPH 4000 ATOM 2204 O2 EPH 4000 24.221 13.543 84.059 1.00 44.96 25.350 11.876 83.028 1.00 47.53 ATOM 2205 O4 EPH 4000 25.126 14.045 81.931 1.00 47.05 ATOM 2206 C18 EPH 4000 ATOM 2207 C19 EPH 4000 24,674 13.569 80.547 1.00 46.98 ATOM 2208 C20 EPH 4000 23,168 13,412 80,473 1,00 49,00 22.772 12.939 79.111 1.00 51.06 ATOM 2209 C21 EPH 4000 21.365 12.327 79.073 1.00 52.88 ATOM 2210 C22 EPH 4000 ATOM 2211 C23 EPH 4000 20.291 13.230 78.423 1.00 54.24 ATOM 2212 C24 EPH 4000 20,651 13,777 77,022 1,00 55,08 ATOM 2213 C25 EPH 4000 19.987 15.129 76.704 1.00 56.13 20.807 16.375 77.147 1.00 56.19 ATOM 2214 C26 EPH 4000 19 981 17 687 77.287 1.00 56.74 ATOM 2215 C27 EPH 4000 ATOM 2216 C28 EPH 4000 19.188 18.077 76.015 1.00 56.93 20.055 18.393 74.792 1.00 57.07 ATOM 2217 C29 EPH 4000 19.294 18.387 73.442 1.00 58.24 ATOM 2218 C30 EPH 4000 19.391 17.124 72.550 1.00 58.70 ATOM 2219 C31 EPH 4000 ATOM 2220 C32 EPH 4000 18.019 16.479 72.198 1.00 59.07 ATOM 2221 C33 EPH 4000 16.762 17.158 72.768 1.00 59.61 ATOM 2222 C34 EPH 4000 15.463 16.541 72.231 1.00 60.17

10

15

20

25

30

35

ATOM 2223 C37 EPH 4000 22.780 13.059 87.421 1.00 47.03 ATOM 2224 O5 EPH 4000 22.047 13.939 88.273 1.00 53.23 ATOM 2225 P1 EPH 4000 21.699 13.222 89.578 1.00 56.71 20.350 13.536 89.939 1.00 58.07 ATOM 2226 O6 FPH 4000 ATOM 2227 O7 EPH 4000 22.579 12.360 90.311 1.00 56.72 ATOM 2228 O8 EPH 4000 22.167 14.340 90.336 1.00 55.93 ATOM 2229 C3 EPH 4000 21.561 15.394 85.253 1.00 42.20 21.886 14.117 85.454 1.00 40.69 ATOM 2230 O1 EPH 4000 ATOM 2231 O3 EPH 4000 22.221 16.347 85.571 1.00 40.97 20.215 15.530 84.546 1.00 40.77 ATOM 2232 C5 EPH 4000 ATOM 2233 C6 EPH 4000 20.313 15.776 83.050 1.00 42.19 ATOM 2234 C7 EPH 4000 18.924 15.916 82.453 1.00 43.05 ATOM 2235 C8 EPH 4000 18.900 15.944 80.947 1.00 44.57 17 477 16 101 80 445 1.00 45 49 ATOM 2236 C9 EPH 4000 ATOM 2237 C10 EPH 4000 17.167 15.209 79.273 1.00 47.18 ATOM 2238 C11 EPH 4000 16.561 15.987 78.117 1.00 47.85 ATOM 2239 C12 EPH 4000 15.158 15.514 77.781 1.00 49.75 ATOM 2240 C13 EPH 4000 15.158 14.254 76.932 1.00 49.27 ATOM 2241 C14 EPH 4000 14 899 14 563 75 454 1.00 51 41 ATOM 2242 C15 EPH 4000 14.958 13.341 74.490 1.00 51.93 ATOM 2243 C16 EPH 4000 16.376 12.870 74.074 1.00 52.39 16.681 11.465 74.554 1.00 52.37 ATOM 2244 C17 EPH 4000 ATOM 2245 C35 EPH 4000 17.830 11.518 75.525 1.00 52.96 ATOM 2246 C36 EPH 4000 17.968 10.168 76.193 1.00 53.00 ATOM 2247 C38 EPH 4000 22.197 10.885 90.057 1.00 56.75 ATOM 2248 C39 EPH 4000 23.458 10.026 89.911 1.00 56.42 ATOM 2249 N1 EPH 4000 24.546 10.825 89.334 1.00 54.45 ATOM 2250 N SER 236 17.914 25.370 86.674 0.50 20.48 AC2 ATOM 2251 CA SER 236 18.176 23.976 86.323 0.50 19.91 AC2 ATOM 2252 CB SER 236 19.157 23.889 85.166 0.50 18.72 AC2 ATOM 2253 OG SER 236 19.325 22.538 84.787 0.50 17.70 AC2 ATOM 2254 C SER 236 18.741 23.171 87.483 0.50 21.62 AC2 ATOM 2255 O SER 236 19.744 23.549 88.075 0.50 20.94 AC2 ATOM 2256 N SER 247 25,235 21,608 79,357 0,50 19,68 AC2 ATOM 2257 CA SER 247 AC2 25.203 22.865 78.619 0.50 20.48 ATOM 2258 CB SER 247 26.051 23.917 79.337 0.50 19.95 AC2

10

15

20

25

30

35

ATOM 2259 OG SER 247 26.032 25.152 78.637 0.50 20.60 AC2 ATOM 2260 C SER 247 25,725 22,638 77,203 0,50 20,84 AC2 AC2 ATOM 2261 O SER 247 25.203 23.202 76.238 0.50 21.05 7.551 30.448 53.176 0.50 29.97 AC2 ATOM 2262 N SER 271 AC2 ATOM 2263 CA SER 271 7.680 31.880 53.442 0.50 31.61 ATOM 2264 CB SER 271 8.888 32.443 52.695 0.50 32.22 AC2 8.666 32.395 51.295 0.50 32.71 AC2 ATOM 2265 OG SER 271 AC2 ATOM 2266 C SER 271 6.432 32.648 53.010 0.50 32.99 6.229 33.796 53.408 0.50 34.05 AC2 ATOM 2267 O SER 271 ATOM 2268 N PRO 319 AC2 18.143 -4.099 74.681 0.50 41.20 AC2 ATOM 2269 CD PRO 319 18.070 -4.311 76.139 0.50 40.63 ATOM 2270 CA PRO 319 18.053 -2.673 74.356 0.50 38.50 AC2 AC2 ATOM 2271 CB PRO 319 17.702 -2.038 75.699 0.50 39.26 ATOM 2272 CG PRO 319 18,406 -2.938 76,680 0.50 39.94 AC2 19.321 -2.077 73.756 0.50 35.96 ATOM 2273 C PRO 319 AC2 ATOM 2274 O PRO 319 20.410 -2.230 74.313 0.50 35.87 AC2 13.913 5.584 80.085 0.50 18.73 AC2 ATOM 2275 N GLN 343 AC2 ATOM 2276 CA GLN 343 12.714 5.137 79.387 0.50 19.83 AC2 ATOM 2277 CB GLN 343 11.463 5.365 80.243 0.50 21.34 10.903 4.078 80.837 0.50 26.09 ATOM 2278 CG GLN 343 AC2 9.539 4.244 81.488 0.50 27.02 AC2 ATOM 2279 CD GLN 343 ATOM 2280 OE1 GLN 343 9.412 4.823 82.562 0.50 29.15 AC2 ATOM 2281 NE2 GLN 343 8.508 3,730 80.829 0.50 29.67 AC2 ATOM 2282 C GLN 343 12.545 5.813 78.025 0.50 19.53 AC2 ATOM 2283 O GLN 343 12.317 5.141 77.022 0.50 19.10 AC2 14.027 4.461 65.783 0.50 19.97 AC2 ATOM 2284 N SER 353 AC2 ATOM 2285 CA SER 353 15,191 3,950 65,107 0,50 20,43 AC2 ATOM 2286 CB SER 353 16.391 4.058 66.033 0.50 20.57 ATOM 2287 OG SER 353 17.540 4.234 65.262 0.50 19.64 AC2 15.054 2.524 64.574 0.50 21.08 AC2 ATOM 2288 C SER 353 ATOM 2289 O SER 353 15.234 2.291 63.378 0.50 21.51 AC2 ATOM 2290 N ARG 392 0.696 20.186 53.122 0.50 19.50 AC2 AC2 ATOM 2291 CA ARG 392 0.935 18.822 53.549 0.50 19.96 ATOM 2292 CB ARG 392 0.325 18.551 54.925 0.50 19.99 AC2 0.603 17.129 55.384 0.50 19.08 AC2 ATOM 2293 CG ARG 392 AC2 ATOM 2294 CD ARG 392 0.140 16.884 56.805 0.50 19.85

10

END

ATOM 2295 NE ARG 392 -1.315 16.885 56.925 0.50 19.23 AC2 ATOM 2296 CZ ARG 392 -1.962 16.577 58.046 0.50 21.63 AC2 ATOM 2297 NH1 ARG 392 -1.283 16.242 59.138 0.50 19.92 AC2 AC2 ATOM 2298 NH2 ARG 392 -3.289 16.611 58.086 0.50 22.19 ATOM 2299 C ARG 392 0.338 17.878 52.501 0.50 19.95 AC2 0.940 16.867 52.149 0.50 20.64 AC2 ATOM 2300 O ARG 392 ATOM 2301 N SER 431 9.466 14.172 75.955 0.50 16.96 AC2 ATOM 2302 CA SER 431 10.735 14.900 76.047 0.50 17.25 AC2 AC2 ATOM 2303 CB SER 431 11.346 15.109 74.659 0.50 17.09 ATOM 2304 OG SER 431 10.765 16.211 73.998 0.50 16.93 AC2 10.466 16.249 76.719 0.50 17.71 AC2 ATOM 2305 C SER 431 ATOM 2306 O SER 431 11.267 16.716 77.521 0.50 17.14 AC2

xlrxrg

pmrxr

lmrxr

smrxr

amusp

tmusp

aarxr

aarxr2

uprxr

Table 2:	
bdrxra	FNEEMPVEKILDAELAVEPKTEAYME
murxra	ANEDMPVEKILEAELAVEPKTETYVE
rnrxra	ANEDMPVEKILEAELAVEPKTETYVE
horxra	ANEDMPVERILEAELAVEPKTETYVE
xlrxra	ANEDMPVEKILEAEHAVEPKTETYTE
surxrb	ANDDIT VIII VIII VIII VIII VIII VIII VIII
aeuspa	VRDVTIERIHEAEQLSEQKSGDNAIPYLR
dmusp	MTNSVSRDFSIERIIEAEQRAETQCGDRALTFLR
horxrb	APEEMPVDRILEAELAVEQKSDQGVEGP
murxrb	APEEMPVDRILEAELAVEQKSDQGVEGP
rnrxrb	APEEMPVDRILEAELAVEQKSDQGVEGP
xlrxrbb	INEEMPVEKILEAELAVEQKSDQSLE
xlrxrba	INEEMPVEKILEAELAVEQKSDQSLE
murxrg	SHEDMOVERILEARLAV
horxrq	CUEDMDVPPII.EAELAVEPKTESYGD
garxrg	CORDMDWRDITEARLAVEPKTEAYSD
xlrxrq	TGRRMDVERIT.EART.AVDPKIEAFGD
pmrxr	DNDDMDVDKTLEARLTSDPKVEOVVP
lmrxr	TUTDMDVFPTT.FAFKPVEE
smrxr	TDT.PNI.TI.PCI.I.SARI.SM
amusp	IHSDMPTERTLEAEKRVECKMEQOGN
tmusp	MOARMDI.DRITEAEKRIECTPAGGSG
aarxr	GADDRMDLERILEARLRVESOTGTLSES
aarxr2	D-GSPDMPLERTLEAEMRVEOPAPSVLAQ
uprxr	ATSDMPTASTREAELSV
cfusp	VOVSDET.STERT.TEMEST.VADPSEEFOFLR
msusp	VORLSTERIJETESLVADPPEEFOFLR
bmusp	VORLSTERLIELEALVADSAEELOILR
ctusp	NGPGRDITVERIMEADOMSEARCGDKSIOYLRV
uspx	AAAORISTERIJEMESIVAAAAEEFOFLR
rxrmin	-ASSANEDMPVEKILEAELAVEPKTETYVE
bdrxra	SSMSNSTNDPVINICQAADKQLFTLVEWAKRIPHFSDLPLDDQVI
murxra	ANMGLNPSSPNDPVTNICOAADKOLFTLVEWAKRIPHFSELPLDDQVI
rnrxra	anmglnpsspndpvtnicoaadkolftlvewakriphfselplddQvi
horxra	ANMGLNPSSPNDPVTNICOAADKOLFTLVEWAKRIPHFSELPLDDQVI
xlrxra	anmglapnspsdpvtnicoaadkolftlvewakriphfsdvplddqvi
surxrb	GSGSSPNDPVTNICOAADKOLFTLVEWAKRIPHFSSLPLDDQVI
aeuspa	VGSNSMTPPEYKGAVSHLCOMVNKOIYOLIDFARRVPHFINLPRDDQVM
dmusp	vgpystvopdykgavsalcovvnkolfomveyarmmphfaqvplddqvi
horxrb	GATGGGGSSPNDPVTNICQAADKQLFTLVEWAKRIPHFSSLPLDDQVI
murxrb	GATGGGGSSPNDPVTNICOAADKQLFTLVEWAKRIPHFSSLPLDDQVI
rnrxrb	GATGGGGSSPNDPVTNICOAADKOLFTLVEWAKRIPHFSSLPLDDQVI
xlrxrbb	GGGSPSDPVTNICOAADKQLFTLVEWAKRIPHFSELALDDQVI
xlrxrba	
murxrq	
horxrg	
garxrg	VNTESSTNDPVTNICHAADKQLFTLVEWAKRIPHFSDLTLEDQVI
arvia	ACI DISTRIDUTAL CHAADKOLETI VEWAKRI PYFSDL PLEDOVI

-----AGLPNSTNDPVTNICHAADKQLFTLVEWAKRIPYFSDL---PLEDQVI

-----FEQVNENDPVSNICKAADRQLVTLVEWAKRIPHFSSL---PLEDQVI

-----CKAENQVEYELVEWAKHIPHFTSL---PLEDQVL

----EAIYEDIPGDDTGLHPLTIICQSIEQQLPRIVNWARQLPVFSSVY-LSFDDQFC

-----YENAVSHICNATNKQLFQLVAWAKHIPHFTSL---PLEDQVL

------GVGEQHDGVNNICQATNKQLFQLVQWAKLIPHFTSL---PMSDQVL

------AQQQDPVSSICQAADRQLHQLVQWAKHIPHFEEL---PLEDRMV

------TAASGRDPVNSMCQAAP-PLHELVQWARRIPHFEEL---PIEDRTA

CSFTLPFHPVSEVSCANPLQDVVSNICQAADRHLVQLVEWAKHIPHFTDL---PIEDQVV

------VGPDSNVPPRYRAPVSSLCQIGNKQIAALVVWARDIPHFGQL---ELDDQVV cfusp ------VGPESGVPAKYRAPVSSLCQIGNKQIAALVVWARDIPHFGQL---ELEDQIL msusp -----VGPESGVPAKYRAPVSSLCQIGNKQIAALIVWARDIPHFGQL---EIDDQIL bmusp -----AASNTMIPPEYRAPVSAICAMVNKQVFQHMDFCRRLPHFTKL---PLNDQMY ctusp -----VGPDSNVPPKFRAPVSSLCQIGNKQIAALVVWARDIPHFSQL---EMEDQIL uspx -----ANMGLNPSSPNDPVTNICQAADKQLFTLVEWAKRIPHFSEL---PLDDQVI rxrmin : :.: :\* \* .: LLRAGWNELLIASFSHRSVTVKDG------ILLATGLHVH bdrxra LLRAGWNELLIASFSHRSIAVKDG-------ILLATGLHVH murxra LLRAGWNELLIASFSHRSIAVKDG------ILLATGLHVH rnryra LLRAGWNELLIASFSHRSIAVKDG------ILLATGLHVH horxra LLRAGWNELLIASFSHRSIAVKDG------ILLATGLHVH xlrxra LLRAGWNELLIASFSHRSIDVRDG------ILLATGLHVH surxrb LLRCGWNEMLIAAVAWRSMEYIETER-----SSDGSRITVROPOLMCLGPNFTLH aeuspa LLKAAWIELLIANVAWCSIVSLDDGGGGGGGGGGHDGSFERRSPGLQPQQLFLNQSFSYH dmusp LLRAGWNELLIASFSHRSIDVRDG-----ILLATGLHVH horxrb LLRAGWNELLIASFSHRSIDVRDG------ILLATGLHVH murxrb LLRAGWNELLIASFSHRSIDVRDG------ILLATGLHVH rnrxrb LLRAGWNELLIASFSHRSISVKDG-----ILLATGLHVH xlrxrbb LLRAGWNELLIASFSHRSISEKDG------ILLATGLHVH xlrxrha LLRAGWNELLIASFSHRSVSVQDG-------ILLATGLHVH murxra LLRAGWNELLIASFSHRSVSVQDG-----ILLATGLHVH horxrq LLRAGWNELLIASFSHRSVSVODG-------ILLATGLHVH garxrg LLRAGWNELLIASFSHRSVSVQDG------ILLATGLHVH xlrxrq LLRAGWNELLIASFSHRSIDVKDS-----ILLASGLHVH pmrxr LLRAGWNELLIAAFSHRSVDVKDG-----IVLATGLTVH lmrxr LIKAAWPELVLISSAYHSTVIRDG------LLLSIGRHLG smrxr LLRAGWNELLIASFSHRSIDVKDG-----IVLATGITVH amusp LLRAGWNELLIAAFSHRSIQAQDA-----IVLATGLTVN tmusp LLKAGWNELLIAAFSHRSVDVRDG-----IVLATGLVVO aaryr LLKAGWNELLIAAFSHRSVAVRDG------IVLATGLVVQ aarxr2 LLKAGWNELLIASFSHRSMGVEDG-----IVLATGLVIH uprxr LIKASWNELLLFAIAWRSMEYLEDER - - - - - - ENGDGTRSTTQPQLMCLMPGMTLH cfusc LIKNSWNELLLFAIAWRSMEYLTDER------ENVD-SRSTAPPQLMCLMPGMTLH msusr LIKGSWNELLLFAIAWRSMEFLNDER-----ENVD-SRNTAPPOLICLMPGMTLH bmusp LI.KOSINELI.IINIAYMSIOYVEPDRRNADG------SLERROISOOMCLSRNYTLG ctusp LIKGSWNELLLFAIAWRSMEFLTAAAAS------PPQLMCLMPGMTLH uspx LLRAGWNELLIASFSHRSIAVK-------DGILLATGLHVH rxrmin \*:: . \*::: : \* hdrxra

RSSAHSAGVGSIFDRVLTELVSKMRDMQMDKTELGCLRAIVLFNPDAKGLSNPSEVEALR RNSAHSAGVGAIFDRVLTELVSKMRDMQMDKTELGCLRAIVLFNPDSKGLSNPAEVEALR murxra RNSAHSAGVGAIFDRVLTELVSKMRDMOMDKTELGCLRAIVLFNPDSKGLSNPAEVEALR rnrxra RNSAHSAGVGAIFDRVLTELVSKMRDMOMDKTELGCLRAIVLFNPDSKGLSNPAEVEALR horxra RNSAHSAGVGAIFDRVLTELVSKMRDMOMDKTELGCLRAIVLFNPDSKGLSNPLEVEALR xlrxra RNSAHSAGVGAIFDRVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPSEVEVLR guryrh RNSAQQAGVDTLFDRILCELGIKMKRLDVTRAELGVLKAIILFNPDIRGLKCQKEIDGMR aeuspa RNSATKAGVSATFDRILSELSVKMKRINLDRRELSCLKATILYNPDIRGIKSRABIEMCR RNSAHSAGVGAIFDRVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPGEVEILR horxrb murxrb RNSAHSAGVGAIFDRVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPGEVEILR RNSAHSAGVGAIFDRVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPGEVEILR rnrxrb RNSAHSAGVGAIFDRVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPGDVEVLR xlrxrbb RNSAHSAGVGATFERVLTELVSKMRDMRMDKTELGCLRAIILFNPDAKGLSNPGDVEVLR xlrxrba RSSAHSRGVGSIFDRVLTELVSKMKDMOMDKSELGCLRAIVLFNPDAKGLSNPSEVETLR murxra horxra RSSAHSAGVGSIFDRVLTELVSKMKDMOMDKSELGCLRAIVLFNPDAKGLSNPSEVETLR RSSAHSAGVGSIFDRVLTELVSKMKDMQMDKSELGCLRAIVLFNPDAKGLSSPSEVESLR garxrq xlrxrq RSSAHNAGVGSIFDRVLTELVSKMKDMDMDKSELGCLRAIVLFNPDAKGLSNAAEVEALR RHSAHOAGVGPIFDRVLTELVSKMRDMMMDKTELGCLRAIVLFNPDVKNLSDSAHIESLR pmrxr RNSAHQAGVGTIFDRVLTELVAKMREMKMDKTELGCLRSVILFNPEVRGLKSAQEVELLR lmrxr REVAKSHGI.GPLVDRII.HEI.VARFRDLSLORTELALLRAIILFNPDANGLSSRHRVEAVR smrxr RNSAQOAGVGTIFDRVLSELVSKMREMKMDRTELGCLRSIILFNPEVRGLKSIQEVTLLR amusp

tmusp aarxr aarxr2 uprxr cfusp msusp bmusp ctusp uspx

bdrxra murxra rnryra horxra xlrxra survrb aeuspa dmusp horxrb murxrb rnrxrb xlrxrbb xlrxrba murxra horxrg garyrg xlrxrq pmrxr lmrxr smrxr amusp tmusp aarxr aarxr2 uprxr cfusp msusp bmusp ctusp

uspx

rxrmin

EKVYASLEGYTKHNYPDOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLEAYCKHKYPEQPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKYYASLEAYCKHKYPEOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLEAYCKHKYPEOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLEAYCKOKYPEOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLETYCKQKYPEQQGRFAKLLLRLPALRSIGLKCLEHLFFFKLI------EKIYACLDEHCKOOHPSEDGRFAQLLLRLPALRSISLKCLDHLNFIRLLSDKHLDSFIVE EKVYACLDEHCRLEHPGDDGRFAQLLLRLPALRS ISLKCQDHLFLFR I TSDRPLEELFLE EKVYASLETYCKOKYPEOOGRFAKLLLRLPALRS IGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLETYCKQKYPEQQGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLETYCKOKYPEOOGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLESYCKOKYPDQQGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYACLESYCKOKYPDOOGRFAKLLLRLPALRS IGLKCLEHLFFFKLIGDTPIDTFLME EKVYATLEAYTKOKYPBOPGRFAKLLLRLPALRS IGLKCLEHLFFFKLIGDTPIDSFLME EKVYATLEAYTKOKYPEOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYATLEAYTKOKYPEOPGRFAKLLLRLPALRS IGLKCLEHLFFFKLIGDTPIDTFLME EKVYATLESYTKOKYPDOPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME EKVYASLEAYCRSKYPDQPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDKFLMN EKVYAALEEYTRTTHPDEPGRFAKLLLRLPSLRSIGLKCLEHLFFFRLIGDVPIDTFLME EOLYSALHSYCTTNOPODTSRFTKLLLRLPPLRS IASKCLEHLVFVKLAAEDPTSCRLIN EKTYGALEGYCRVAWPDDAGRFAKLLLRLPAIRS IGLKCLEYLFFFKMIGDVPIDDFLVE EKIYGVLEBYTRTTHPNEPGRFAKLLLRLPALRSIGLKCSEHLFFFKLIGDVPIDTFLME ESV-SALEEHCRQQYPDQPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDNFLLS EKVYAALEEHCRRHHPDQPGRFGKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDSFLLN EKVYAALEEYTRTTYPDEPGRFAKLLLRLPALRSIGLKCLEYLFLFKLIGDTPLDSYLMK EKMFSCLDDYCRRSRSNEEGRFASLLLRLPALRSISLKSFEHLYFFHLVAEGSISGYIRE EKMFSCLDEYVRRSRCAEEGRFAALLLRLPALRSISLKCFEHLYFFHLVADTSIASYIHD EKMFLCLDEYCRRSRGGEEGRFAALLLRLPALRSISLKSFEHLYLFHLVAEGSVSSYIRD SRIYASLDEYCROKHPNEDGRFAQLLLRLPALRSISLKCLDHLFYFQLIDDKNVENSVIE EKMFLCLDEYCRRSRSSEEGRFAALLLRLPALRSISLKSFEHLFFFHLVADTSIAGYIRD EKVYASLEAYCKHKYPEQPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLME : .\*\* \*\*\*\*\*\*.:\*\*\*. \*. ::\*

bdrxra MLEAPHQIT murxra MLEAPHOAT MLEAPHOTT rnrxra horxra MLEAPHOMT xlrxra MLEAPHOMT surxrb MI-DMPI --aeuspa QLEAPPPPG dmusp horxrb MLEAPHOLA muryrh MLEAPHOLA rnryrh MI.EAPHOLA xlrxrbb MLEAPHOLS xlrxrba MLEAPHOLS MLETPLQIT murxrq MLETPLOIT horxrq garxrg MLETPLOVT xlrxrq MLETPHOIS

1
10
0
127
1.13
U
T
-
1
741
Seed.
Seed .
L

pmrxr	MLETTSDFP
lmrxr	MLESPSDS-
smrxr	LVEHGVWPI
amusp	MLESRSDP-
tmusp	MLESPADA-
aarxr	MLEAPSDP-
aarxr2	MLEAPADP-
uprxr	MLVDNPNTS
cfusp	ALRNHAPPI
msusp	ALRNHAPSI
bmusp	ALCNHAPPI
ctusp	EPHKLN
uspx	ALRNGG
rxrmin	MLEAP

## References

5

10

15

20

- Oro A.E. et al. (1990): Relationship between the product of the Drosophila ultraspiracle locus and the vertebrate retinoid X receptor. Nature 347, 298-301
  - Moras D. & Gronemeyer H. (1998): The nuclear receptor ligand-binding domain: structure and fiction. Current Opinion in Cell Biology 10, 384-391
  - Segraves W.A. (1994): Steroid Receptors and Other Transcription Factors in Ecdysone Response. Recent Progress in Hormone Research, 49, 167-195
  - Henrich V.C. & Brown N.E. (1995): Insect Nuclear Receptors: A
    Developmental and Comparative Perspective. Insect Biochem. Mol. Biol. 25
    (8), 881-897
  - Thummel C.S. (1995): From Embryogenesis to Metamorphosis: The Regulation and Function of Drosophila Nuclear Receptor Superfamily Members. Cell 83, 871-877
  - Truman J.W. (1996): Ecdysis Control Sheds Another Layer. Science 271, 40-41
  - Yao T. et al. (1993): Functional ecdysone receptor is the product of EcR and Ultraspiracle genes. Nature 366, 476-479
  - Hall B.L. & Thummel C.S. (1998): The RXR homolog Ultraspiracle is an essential component of the Drosophila ecdysone receptor. Development 125, 4709-4717
- Lezzi M. et al. (1999): The Ecdysone Receptor Puzzle. Arch. Insect Biochem.
   Physiol. 41, 99-106
  - Mikitani K. (1996): Ecdysteroid Receptor Binding Activity and Ecdysteroid Agonist Activity at the Level of Gene Expression are Correlated with the Activity of Dibenzoyl Hydrazines in Larvae of Bombyx mori. J. Insect Physiol. 42 (10), 937-941
- Dhadialla T.S. et al. (1998): New Insecticides with Ecdysteroidal and Juvenile Hormone Activity. Annu. Rev. Entomol. 43, 545-569

10

20

30

- 96 -
- Sundaram M. et al. (1998): Basis for selective action of a synthetic molting 12. hormone agonist, RH-5992 on lepidopteran insects. Insect Biochem. Mol. Biol. 28, 693-704
- Rarey M. et al. (1996): Predicting Receptor-Ligand Interactions by an 13. Incremental Construction Algorithm. J. Mol. Biol. 261(3), 470-489
- Jones G. et al. (1997): Development and Validation of a Genetic Algorithm 14. for Flexible Docking, J. Mol. Biol. 267 (3), 727-748
- Böhm H.J. (1992): LUDI: Rule-Based Automatic Design of New Substituents 15. for Enzyme Inhibitor Leads. J. Comp.-Aided Mol. Design 6, 593-606
- Nishibata Y. & Itai A. (1991): Automatic creation of drug candidate 16. structures based on receptor structure. Starting point for artificial lead generation. Tetrahedron 47, 8985-8990
  - Moon J.B. & Howe W.J. (1991): Computer design of bioactive molecules: a 17. method for receptor-based de novo ligand design. Proteins 11 (4), 314-328
- Otwinowski Z. & Minor W. (1997): Processing of X-ray diffraction data 15 18. collected in oscillation mode. Methods Enzymol. 276, 307-326
  - Navaza J. (1994): Amore: an automated package for molecular replacement. 19. Acta Cryst. A 50, 157-163
  - Egea P.F. et al. (2000): Crystal structure of the human RXRalpha ligand-20. binding domain bound to its natural ligand 9-cis retinoic acid. EMBO J. 19, 2592-2601
  - Jones T.A. et al. (1991): Improved methods for generateing protein models in 21. electron density maps and the location of errors in these models. Acta Cryst. A 47, 110-119
- Perrakis A. et al (1997): wARP: improvement and extension of crystallo-25 22. graphic phases by weighted averaging of multiple-refined dummy atomic models, Acta Cryst, D 53, 448-455
  - Brünger A.T. et al. (1998): Crystallography & NMR System: A New 23. Software Suite for Macromolecular Structure Determination. Acta Cryst. D 54, 905-921

 Laskowski R.A. et al. (1993): PROCHECK:a programme to check the stereochemical quality of protein structure coordinates. J. Appl. Crystallogr. 26, 283-291